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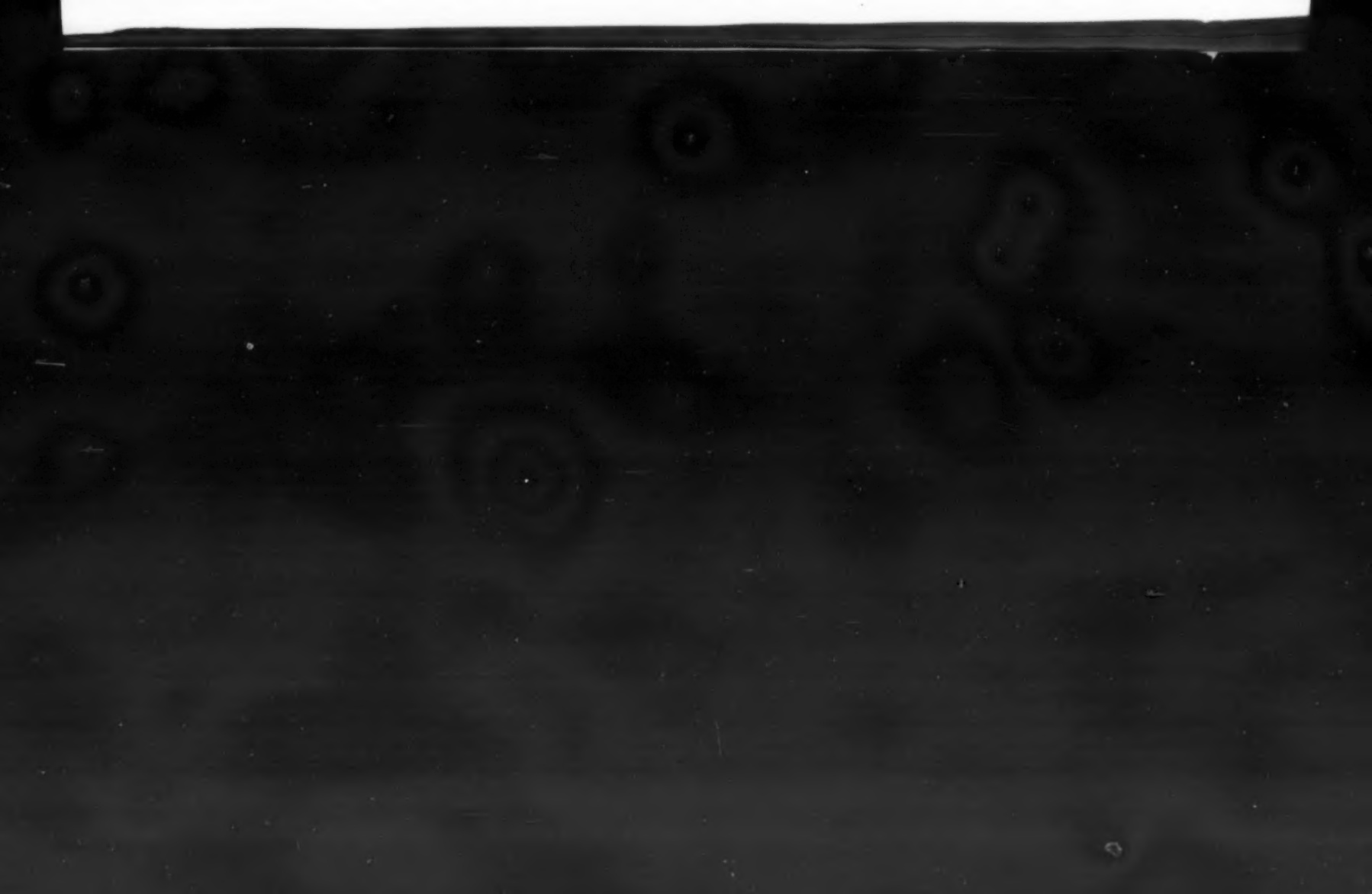

The Journal of Pediatrics

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Original Communications

PULMONARY INFILTRATION AND BLOOD EOSINOPHILIA IN CHILDREN (LOEFFLER'S SYNDROME)

A REVIEW WITH REPORT OF EIGHT CASES

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NEW YORK, N. Y.

IN 1932[1] and again in 1936,[2] Loeffler described a syndrome characterized by transitory pulmonary infiltrations, eosinophilia, and a benign course with few symptoms. Subsequent publications described patients with more severe symptoms and a prolonged course.

An increasing number of etiological agents is being suggested. The mounting interest in Loeffler's syndrome arises from the recognition of its allergic background, and its frequent association with helminthiasis. In the New York area, especially, many cases are associated with intestinal parasitism owing to the influx of Puerto Ricans and the return of veterans from areas infested with helminthiasis.

Seven patients presenting the picture of Loeffler's syndrome associated with intestinal parasitism are here reported. Two of these were unusual because of the chronicity of the syndrome.

The clinical course originally described by Loeffler lasted two to three weeks, and was characterized by malaise, slight nonproductive cough, and low-grade fever, although 60 per cent were afebrile. Chest signs were few, often only a few crepitant râles, and a mild leucocytosis with eosinophiles ranging from 6 to 66 per cent. The extent of the pulmonary pathology was in marked contrast to the clinical course. The pulmonary densities had no distinctive features, appearing as single or multiple shadows in one or both lungs. Loeffler emphasized the fleeting nature of the lesions with sudden appearance and disappearance in three to eight days. Occasionally there was a pleural reaction with a small basal effusion.

Because cases have been subsequently reported of greater severity and chronicity, Kartagener[3] suggested the recognition of three forms of pulmonary infiltration with eosinophilia, namely, the transient type with mild symptoms as described by Loeffler, an acute and severe type with lesions as described by Löhr

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and Leon Kindberg,[3] and a third group reported by Kartagener, characterized by chronicity and mildness of symptoms. These three types, he believed, represented variants of the same disease.

ETIOLOGY

In Loeffler's second report, the allergic nature of the syndrome was first mentioned and the similarity to the pathogenesis of erythema nodosum was noted. The transient pulmonary infiltrates appeared comparable to a visceral erythema nodosum.

Alpher[4] divided the exciting factors into two groups: extrinsic (plant pollens such as privet[5] or Maiglöckchen,[6] and sulfonamides) and intrinsic (associated with infection, such as tuberculosis, brucellosis, amebiasis, and infestations with ascaris, necator, *Fasciola hepatica,* and *Ancylostoma braziliense*).

1. Privet Allergy.—Engel,[5] in 1936, first offered substantial evidence of the allergic basis of Loeffler's pneumonia. In May and June many patients became ill with a peculiar bronchitis called privet cough. Privet, a species of ligustrum, flowers in these months. The bronchitis was characterized by a moderately severe cough with a scanty, canary yellow sputum containing a few leucocytes and microbes, and associated with pulmonary x-ray shadows lasting one to six days. The eosinophilia was 20 to 25 per cent. The seasonal incidence, transient pulmonary infiltration, and the eosinophilia suggested the allergic genesis of the condition.

2. Other Allergies.—Transitory pulmonary lesions with eosinophilia have been observed in patients with asthma.[7, 8, 9, 10] Harkavy[11] studied sixteen patients with asthma and chronically infected sinuses, who also had other typical allergic reactions in the skin, pleura, pericardium, peritoneum, synovial membranes, and bone marrow. A high eosinophilia was noted in the blood and serous exudates of these patients. Harkavy suggested that the underlying process was an hyperergic response of the blood vessels and mesodermal tissues to an antigen such as bacteria, toxins, or viruses in an allergic individual.

In fifty-two of 100 cases of Loeffler's pneumonia, Maier[12] described other allergic phenomena such as eczema, hay fever, migraine, vascular rhinitis, and urticaria. Sensitivity to bacteria causing upper respiratory infections is another allergic basis for Loeffler's pneumonia. Hansen-Pruss and Goodman[8] reviewed six cases of this type, all demonstrating the following characteristics: varying degrees of pulmonary involvement clinically and in the x-rays, an allergic background, varying leucocytosis and eosinophilia, an afebrile clinical course, persistent, severe asthma, lack of response to the sulfonamides, and a history of frequent upper respiratory infections. In these patients the sputum contained many eosinophiles.

3. Tropical Eosinophilia.—Frimodt-Möller and Barton,[13] in 1940, first described tropical eosinophilia which resembled Loeffler's syndrome. Subsequently, reports from tropical countries, particularly India,[14] Singapore,[5] and Australia[15, 16] appeared. These cases were also called pseudotuberculosis with eosinophilia. The disseminated mottling revealed in the lung x-rays lasted about four

weeks. Frequent morning paroxysms of asthma, fever, weakness, loss of appetite and weight, and, commonly, splenomegaly were observed. There was marked leucocytosis and eosinophilia with respective maximums of 80,000 and 80 per cent. The etiology was unknown, but the common climatic and geographic factors led to the designation, tropical eosinophilia. The sputum of patients studied in Ceylon contained a cheese mite.[17] The asthmatic attacks, the eosinophilia, and the occasional findings of eosinophiles in the sputum suggested an allergic basis. Tuberculosis, syphilis, and heart disease were ruled out, although Weingarten's[14] cases cleared rather promptly after therapy with arsenic.

4. Helminthiasis.—A growing volume of literature emphasizes the importance of helminthiasis in the production of Loeffler's syndrome. Wild, of Basle,[18] particularly stressed this pathogenic agent when he reported fourteen children with this syndrome, four of whom had ascaris ova in their stools.

Clinical observations and experiments have demonstrated during the migration of ascaris larvae through the human body, pulmonary perifocal reactions producing transitory roentgen shadows. Frimodt-Möller and Barton[13] cite Muller's experience with four physicians, who, after eating salad which grew in soil infested with ascaris, developed a Loeffler's syndrome. Muller confirmed the etiology by swallowing three tablespoonsful of the contaminated soil, thereby reproducing the picture in himself eight days later. Koino[19] fed 500 ascaris ova to a healthy man. A few days later dry and moist râles appeared in the chest. Koino duplicated this experiment in himself by swallowing 2,000 ova of ascaris which produced pneumonic consolidations and sputum containing larvae. Beck[20] reported a classical case of Loeffler's syndrome with *Ascaris lumbricoides* and *Strongyloides intestinalis* in the stools. Treatment with Crystoids of hexylresorcinol caused prompt and marked improvement with disappearance of the urticaria and regression of the pulmonary infiltration.

Quintana[21] believed that the toxic metabolites of *Necator americanus* are allergenic factors in producing Loeffler's syndrome. He described such a case in a 14-year-old white male with a chronic history of symptoms, and pulmonary infiltrations in the base of the left lung all of which cleared in thirteen days following antihelminthic therapy.

Another parasite, *A. braziliense,* has caused transient pulmonary infiltration of the Loeffler type. Wright and Gold[22] reported nine such cases associated with cutaneous creeping eruption due to nematode infection of the skin. Intradermal tests with extracts of this ancylostome were positive.

Slowey[23] described a case of transient, successive pulmonary infiltrations which he attributed to an allergic reaction in the bronchi and interstitial lung tissues caused by *Trichinella spiralis.*

Grayce[24] described a 26-year-old woman whose chest x-ray revealed a small, oval, ill-defined opacity in the right midzone suggestive of pulmonary tuberculosis, but the gastric contents and sputum were negative for the tubercle bacillus. There was no allergic history. Blood count showed a white blood count of 17,500 with 62 per cent eosinophiles. *Trichuris trichiura* was repeatedly found in the

stools. The chest x-ray remained clear after the nineteenth day. After treatment for the infestation, a moderate drop in the eosinophilia was observed which several months later fell to 3 per cent.

Asthmatic attacks and pulmonary infiltration persisted for four months in a patient reported by Hoff and Hicks,[25] but cleared dramatically after *Endamoeba histolytica* infestation was discovered, and specific therapy instituted. Stefano[26] reported a similar case in which amoebae were found in the sputum but not in the stools. The amoebae, asthma, and lung shadows also disappeared after a course of emetine.

Whitehouse[27] reported two cases of massive eosinophilia in uncomplicated uncinariasis. The eosinophiles in one amounted to 71 per cent and gradually declined to almost normal in fifty-six days after successful treatment. In the second patient, the eosinophilia fell slowly from 66 per cent to 7 per cent in thirty-eight days.

It has been noted also by other observers that the eosinophilia persists for one to two months after the stools have become negative for ova and parasites.

5. Tuberculosis.—A causal relationship between tuberculosis and Loeffler's syndrome was repeatedly suggested by some of the pulmonary x-ray shadows, the infraclavicular lesions, and the small, multiple, disseminated lesions. Loeffler studied the tuberculous background of his patients and found that twenty-four of the fifty-one had positive Mantoux tests. He concluded that in some of these the syndrome was related to tuberculosis and that the x-ray shadows were early tuberculous infiltrations associated with eosinophilia as a manifestation of tuberculous hypersensitivity.

Söderling[7] noted that patients recently infected with tuberculosis may show transient lung changes which are not true bacillary infiltrations but are tuberculin-allergic manifestations similar to that described by Loeffler.

Many patients with Loeffler's syndrome have been erroneously diagnosed as having pulmonary tuberculosis. Karan and Singer[28] described five such cases with eosinophilia and transient pulmonary infiltrates in one of which the roentgen shadows migrated for three months. The original diagnosis of pulmonary tuberculosis was later discarded since the infiltrates were transient and the tuberculous etiology was unconfirmed. Pirkle and Davin[29] also described a case misdiagnosed as pulmonary tuberculosis with pneumonitis migrating for eight months.

The frequency and degree of eosinophilia and its etiological relation to tuberculosis was studied in the Union Mission Sanatorium.[15] Between 1925 and 1947, 600 patients were admitted to this Sanatorium with a diagnosis of pulmonary tuberculosis. One hundred seventy-five of these had a blood eosinophilia of 20 to 92 per cent and pulmonary x-ray changes of extensive bilateral mottling by small nodular shadows and increased hilar markings. The general appearance was that of miliary tuberculosis or silicosis. Of these cases, 69 per cent were tuberculin-negative and none had positive sputa. Intestinal infestations were found in 48 per cent. However, these 175 patients differed from the original Loeffler's syndrome in that their lung lesions were not transitory. Of the remainder of the 600 patients, 194 had tubercle bacilli in their sputa and many

showed eosinophilia to 20 per cent. A correlation study of eosinophilia and positive sputa showed that the percentage of positive sputa decreased rapidly as the eosinophiles increased. No case with eosinophilia under 20 per cent showed the characteristic miliary mottling in the x-ray described in the Loeffler's pneumonia.

The evaluation of the relationship of tuberculosis to Loeffler's syndrome requires a consideration of the role of the eosinophile "in the tuberculin type of sensitivity established during bacterial infection." Rich[30] claimed that it played no role whatever. There was no eosinophilia in the circulating blood nor in the site of hypersensitive reactions produced by the tubercle bacilli or tuberculoprotein. Clinical studies, on the other hand, offered different evidence. Müller[31] studied 1,000 patients with pulmonary tuberculosis in various stages of the disease and found in 9.0 per cent of the patients an eosinophilia of over 6 per cent. In contrast to the findings in Loeffler's syndrome, most cases of which showed 20 per cent or more eosinophiles, only 0.2 per cent of Müller's patients had eosinophilias over 15 per cent. She and many other observers considered that the variation in eosinophiles found in tuberculosis was an expression of allergy equivalent to that found in other allergic diseases such as asthma, hay fever, and urticaria.

Henderson and Peirce[32] emphasize how impossible it is to view any single film in cases of transitory focal pulmonary infiltration and eosinophilia without being immediately impressed with the possibility of tuberculous origin. Although eosinophilia may be associated with early tuberculous lesions, it is usually not more than 4 to 7 per cent and never reaches the high proportions found in Loeffler's syndrome.

6. Other Agents.—Willett and Oppenheim[33] described coccidioidomycosis in three patients with 27 to 89 per cent eosinophiles in the blood. One of these, whose eosinophilia reached 89 per cent, showed a disseminated coccidioidomycosis involving lymph nodes and skin, as well as the lungs. Examination of the chest was negative although the lung x-ray revealed a diffuse granular density which cleared in two months.

Elsom and Ingelfinger[34] reported two cases with *Brucella abortus* infection which they believed to be the allergen. These patients had fever, pneumonitis, eosinophilia, and an immune response to Brucella.

In summary, it appears that Loeffler's eosinophilic pneumonia is an allergic response of the lung to a variety of agents, extrinsic such as the privet plant, or intrinsic such as helminths, and tuberculosis. Occasionally, the condition is associated with bacterial infections.

PATHOLOGY

Loeffler's syndrome is a mild disease and fatality is rare, hence reports of pathology are scarce. Von Meyenburg[35] first described the findings in four patients in the military service. Three of these died accidentally and the fourth died of tetanus. The pulmonary infiltrate consisted principally of eosinophiles which were present both in the alveoli and the interstitial tissues with inflammation of the pleura. Two of the four patients had eosinophilic infiltration in the liver, spleen, the bronchi and bronchioles.

Bayley and collaborators[36] described the pathologic examination of the lungs only in a patient with chronic Loeffler's pneumonia as follows: There was a scattered adhesive pleurisy and about 300 c.c. of serosanguinous fluid in each pleural cavity. The pneumonic exudate showed a predominance of eosinophiles with advanced organization. Granulomatous, tubercle-like lesions with occasional giant cells were seen. There were necrotizing arteritis and phlebitis. The bronchial lesions resembled those of asthma, with an eosinophilic exudate infiltrating all portions of the wall. The thickening and hyalinization of the pneumonic exudate and the granulomatous character of the tubercle-like lesions indicate that the pulmonary lesions are not always transitory. Fibrinoid swelling and necrosis of collagen were prominent features which with the large number of eosinophiles, and the necrotizing arteritis, similar to periarteritis nodosa, further suggest the allergic basis of Loeffler's syndrome. Guinea pig studies and cultures were negative for *Mycobacterium tuberculosis.*

Recently, Loeffler, Essellier, and Macedo[47] reproduced the clinical syndrome described in man by feeding fairly large amounts of ascaris larvae to guinea pigs. When the infestation was heavy, the animals died, otherwise they were killed at varying times following the initial infestation. All organs were studied. The most extensive changes appeared in the lungs. Two types of lesions were found, eosinophilic exudate in the parenchyma, around blood vessels and bronchi, and areas of atelectasis often adjoining these lesions. No pleural exudate was found but there were frequent changes of the pleura in areas immediately adjoining eosinophilic infiltrations. There was swelling of the epithelial cells and desquamation of the visceral pleura. These observations support Loeffler's previous descriptions of the clinical occurrence of pleurisy. Eosinophilic infiltrations with foci of hemorrhage and necrosis was described in the liver where often ascaris larvae were found. Eosinophilia was regularly seen in the bone marrow, spleen, tracheal and mesenteric lymph nodes.

These lesions were temporary; guinea pigs sacrificed thirty-four days after the first infestation showed no pathologic change. The extent of the lesions found was correlated with the duration of infestation. The more recent infestations showed the more extensive changes.

PATHOGENESIS

The pathologic lesions described support the allergic theory. As noted, Loeffler believed that the pulmonary change was analagous to erythema nodosum and was therefore comparable to, or, in some instances, actually in the nature of, a tuberculid of the lungs. Alpher[4] believed that the pulmonary interstitial tissue served as the shock organ in the allergy of Loeffler's pneumonia as do the terminal bronchial units in asthma. Adrenalin does not alter the lung signs in Loeffler's syndrome, although the eosinophilia may be reduced. Maier[12] was also convinced that the lung picture in his patients was allergic since a majority displayed manifest allergic signs concomitantly in other tissues. Hansen-Pruss and Goodman[8] supported this theory in their report of six patients who had allergic responses to nonspecific bacteria, with frequent upper respiratory in-

fections. There was no response to sulfonamides, and the asthma persisted until the pulmonary shadows cleared. Smith and Alexander[10] also stressed the causative role of bacterial allergens.

Engel[5] considered the lung changes in his patients with privet cough as Quincke's edema and suggested the name "edema allergicum pulmonis." Cole and Korns[37] considered the syndrome as presumably due to angioneurotic edema of the lungs.

Söderling[7] believed that the pulmonary infiltrations were localized areas of atelectasis and emphysema produced by the stagnant secretions of bronchitis combined with bronchial spasm. In severe asthma, these localized areas cast transient, parenchymal shadows. He also suggested the same pathology may be present in many cases of atypical pneumonia and abortive pneumonia, so-called "one day pneumonias," and even in the rapidly recovering pulmonary tuberculosis in tuberculin-positive patients. He emphasized the transient nature of the consolidations, "usually a matter of hours." But the pathologic study of von Meyenburg revealing an eosinophilic exudate in the parenchyma of the lung, refutes Söderling's idea of atelectasis and emphysema as the *sole* change in the lungs.

In patients with helminthiasis, attempts were made to differentiate the eosinophilia due to the allergic pulmonary factor from that due directly to the parasitic infestation. It has been claimed that the granules of the eosinophiles in the Loeffler's syndrome are larger.[49] A careful study of eosinophiles in Case 3 by one of us failed to reveal any qualitative change in eosinophiles either in the peripheral blood or bone marrow. There were no distinguishing characteristics in any of the blood cells. None of these factors was of significant differential value. However, more massive and prolonged eosinophilia was found in some cases of Loeffler's syndrome with helminthiasis in which liver damage with eosinophilic infiltration occurred.

Perlingiero and György[38] reported a case of chronic eosinophilia with necrosis of the liver, pulmonary infiltration, anemia, and ascaris infestation in a 2-year-old Negro boy known to be allergic. Fourteen months after onset of pulmonary disease, the eosinophilic count was 34 per cent, while all else was normal. Laparotomy for intestinal obstruction revealed an enlarged liver with numerous small, gray-white lesions covering its surface. Biopsy showed that these lesions consisted of focal necrosis with many polymorphonuclear leucocytes, eosinophiles, and multinucleated giant cells. Liver damage was evidenced by low serum protein, later rising to 10.9 Gm., a reversal of the serum albumin-globulin ratio, and a cephalin flocculation of 3+. A false-positive serologic test for syphilis was associated with the increase in gamma globulin. These blood findings gradually returned to normal at which time a second liver biopsy showed a return to normal structure.

Zuelzer's[45] recent report of liver biopsy or autopsy in four patients who showed prolonged eosinophilia of the blood and bone marrow, as well as hyperleucocytosis, hyperglobinemia, and a variable clinical picture, confirms the pathogenesis and pathology of this condition. He also holds the opinion that the so-called Loeffler's syndrome is an allergic hyperergic tissue response to undeter-

mined antigens. The hepatic pathology of necrosis, granuloma formation, and severe eosinophilic infiltrations corresponded to the lung changes in Loeffler's syndrome.

In Harkavy's[11] patients with asthma and chronically infected sinuses, the pulmonary lesions were insidious in onset, migratory, miliary, and interstitial in distribution, and occasionally exudative, simulating tuberculosis. However, these patients differed from Loeffler's original description in the more prolonged duration of the infiltration, and in the occasional appearance of large pleural effusions requiring aspiration and containing from 85 to 100 per cent eosinophiles. Biopsy of the skin lesions in three cases (two from purpuric areas and one from a necrotic lesion) showed perivascular eosinophilic infiltration. In one case the biopsy of a subcutaneous nodule, in addition, showed infiltrations indistinguishable from those seen in periarteritis nodosa.

Harkavy suggested that any tissue may be involved in the allergic response. The clinical syndrome depends on the degree of involvement and the shock tissue affected. The pathologic changes may or may not be reversible, and the ultimate picture may be periarteritis nodosa. Harkavy further emphasized the allergic theory by quoting Danziger's case of a boy with periarteritis nodosa who was given an injection of minute quantities of a vaccine prepared from washings of his own sinuses. Within twenty-four hours he developed signs of pulmonary infiltration and generalized purpura.

In discussing prognosis, Harkavy emphasized that when bacterial hyperergy complicated an asthma due to the usual allergens, a disease more severe than Loeffler's may result. Transient lung infiltrations with eosinophilia may be a warning in such cases of an impending generalized vascular allergy with panarteritis as an eventual outcome. Therefore, foci of infection must be eradicated, especially chronically infected sinuses.

Rich and Gregory,[39] in their extensive work on allergy, point out that the eosinophiles are not always present in allergic reactions as in anaphylactic pneumonitis and in urticarial lesions. Therefore the absence of peripheral eosinophilia, especially if not repeatedly studied, does not rule out an allergic reaction in the lung, as in Loeffler's syndrome.

Of the many helminths studied,[23, 40, 41] ascaris has been most frequently associated with Loeffler's syndrome. Müller[31] believed that the x-ray shadows were caused directly by the passage of the ascaris larvae through the lungs after they had penetrated the intestinal wall and travelled into the liver. Koino[19] demonstrated the same facts in his experimental production of ascariasis. Keller and collaborators[42] also showed that the migration of ascaris larvae through the lungs caused pulmonary inflammation either directly or indirectly, by favoring secondary invasion by microorganisms. He studied eighty Tennessee children with ascariasis and found that many of them had increased hilar and bronchovascular markings. Except for the absence of calcification their x-ray shadows resembled those seen in children with positive tuberculin tests who were studied simultaneously.

Both Beck[20] and Quintana [21] theorize that the helminths produce the lung changes only indirectly by causing an allergic reaction due to their presence in

TABLE I. STUDY OF POSSIBLE ETIOLOGIC FACTORS IN EIGHT PATIENTS

CASE RACE AGE	PROBABLE ETIOLOGY	TUBERCULIN TESTS	HISTORY OF ALLERGY	STOOLS	CUTANEOUS TESTS	OTHER TESTS	COMMENT
1. *N. A.* P. R. 13 yr.	Int. parasite	Mantoux + 1:10,000	Asthma from 6-11 yr. of age in P.R. None past 2 yr. in New York City	Ova of *N. americanus*	Not done	Typhoid, Paratyphoid, Brucellosis } neg.	Sputum and gastric cultures repeatedly negative for *Myco. tuberculosis*
2. *J. C.* Negro 19 yr.	Int. parasite	Mantoux + 1:1,000	Neg.	Ova of *N. americanus*	Not done		Sputa and gastrics neg. for TBC
3. *A. W.* P. R. 10 yr.	Int. parasite	Tuberculin patch +	Neg.	1 male ascaris passed; ova of *G. lamblia* and *T. trichiura*	Trichinella neg. 24 hr.; histoplasmin coccidioidin and schistosoma – (1:500 H antigen)	Typhoid agglut. 1:160 +; paratyphoid 1:160 +; proteus neg.; brucella neg. Trich. PPT test + 1:320. Schistosoma PPt test –	
4. *J. C.* P. R. 4 yr.	Int. parasite	Mantoux neg. 1 mg.	Neg. but poor history. Father does not know history between 1-3½ yr. while in Puerto Rico	+ for ascaris, ancylostoma, giardia, trichiura *Endolimax nana*			Barium meal x-ray of intestines outlines ascarids
5. *V. C.* P. R. 8 yr.	Int. parasite	Mantoux neg. 1 mg.		+ for ancylostoma and trichuris			
6. *N. R.* P. R. 12 yr.	Int. parasite	Patch +		+ for schistosomiasis; strongyloidiasis; trichuris	Trichinelli neg.		Hepatomegaly marked; transient—lung signs. No evidence of pulmonary TBC
7. *J. Q.* P. R. 7 yr.	Int. parasites	Neg. patch		*A. lumbricoides* *T. trichiura*	Not done		Laparotomy performed for R.L.Q. mass and terminal ileum found to be injected, edematous and presumably containing parasites. Microscopic section of appendix showed numerous parasites
8. *A. M.* P. R. 11 yr.	Bacterial from paranasal sinuses	Neg. patch		Repeatedly neg. for ova and parasites. History of parasites 7 yr. previously.	Trichinella neg.	Cephalin flocculation strongly positive	Gastric washings neg. for *Myco. tuberculosis.* Marked clouding of ethmoid and maxillary sinuses by x-ray.

the host's body. However, another mechanism, that of inhalation, in producing allergy was cited by Baer.[43] He described the experience of a zoologist who developed severe rhinitis and conjuctivitis when he walked through a laboratory in which ascarids were being studied.

CASE REPORTS

CASE 1.—N.A., Sea View No. 30939, a Puerto Rican male, was 13 years old. He had "asthmatic attacks" during the summer from 5 to 11 years of age until he arrived in this country in the spring of 1945. In November, 1946, he developed a cough, wheezing respiration, and low-grade fever.

Family History.—The father died of pulmonary tuberculosis when the patient was 1 year old. The mother had asthma in childhood. One older sibling has a history suggestive of rheumatic fever.

Present History.—In December, 1946, the patient was admitted to a New York City hospital where a positive Mantoux test was found and repeated chest x-rays revealed "fine miliary infiltrations, larger than the usual." Repeated gastric washings and laryngoscopic smears were negative for acid-fast organisms. Blood eosinophilia was 36 per cent. Stool examinations were negative for ova and parasites. The patient soon became asymptomatic except for a low-grade fever. After eight months of bed rest, he was sent to Sea View Hospital with a diagnosis of chronic miliary tuberculosis.

Physical Examination.—On admission to Sea View Hospital on July 15, 1947, the patient did not appear ill. Medium moist and large dry râles were heard throughout both lungs. The blood pressure was 110/60. The liver and spleen were not palpable. Pea-sized lymph nodes were felt in both axillary and inguinal regions.

Laboratory Findings on Admission.—A chest x-ray showed extensive hypervascularization, with increased prominence of the bronchovascular markings, and fine, stippled, disseminated shadows. There were some exudative, productive changes in the right upper lobe, and increased prominence of the hilar shadows bilaterally as a result of enlargement of the tracheobronchial lymph nodes.

Blood studies revealed hemoglobin, 79 per cent; 4,000,000 erythrocytes and 29,850 leucocytes per cubic millimeter, with 9 per cent segmented polymorphonuclear cells and 5 per cent nonsegmented, 21 per cent lymphocytes, and 65 per cent eosinophiles. The erythrocyte sedimentation rate was 39 c.mm. per hour, the blood nonprotein nitrogen 39.5 mg. per cent, and the proteins were normal. The urine was negative. The Mantoux test was positive to 1:10,000. Gastric washings and feces contained no acid-fast organisms. *Ova of N. americanus were found in the stools.* A sternal puncture showed normal cytology.

Clinical Course.—On the eleventh hospital day, 0.8 Gm. of hexylresorcinol was given. Twelve days later, the stools became negative for ova and remained so for eight weeks. Treatment with hexylresorcinol was repeated when ova appeared again in the stools. Thereafter, the stools remained negative for two and one-half months, when the patient was discharged.

Eleven days after the first course of treatment, chest x-rays showed a considerable resolution of the widespread infiltration. The prominent vascular shadows had become normal. Coincidentally, the râles had also disappeared and the white count had dropped to 13,100 and the eosinophiles to 44 per cent (Table II). Sputum eosinophilia persisted until the time of discharge, decreasing as the pulmonary shadows cleared.

On the forty-first hospital day, a flare-up followed the administration of an expectorant cough mixture given to raise sputum for examination. There was a slight productive cough. Coarse and medium moist râles were heard. Within two weeks the episode had subsided and the chest cleared.

TABLE II. STUDY OF BLOOD PICTURE CORRELATED WITH ROENTGENOGRAMS AND INTESTINAL PARASITIC INFECTION (CASE 1)

DATE	HB. GM.	R.B.C.	W.B.C.	POLYS. %	LYMPHS. %	MONOS. %	EOSINO. %	EOSINO. TOTAL	FECES FOR OVA AND PARASITES	TREATMENT FOR PARASITES	X-RAYS
7/16/47	11.0	4,020,000	26,350	4	20	0	59	15,546	Pos. for ova, 7/18, 7/23	Hexylresorcinol 0.8 Gm. 7/26	+++ disseminated miliary mottling; dense shadow RUL; ++ inc. prominence of bronchovascular markings
to	to	to	to	to	to	to	to	to			
7/26/47	11.6	4,100,000	29,850	13	27	3	65	19,402			
7/28/47	11.5	4,050,000	10,500	1	15	2	17	2,329	Pos. for ova 7/28, 7/30, 8/3, 8/6		+ disseminated mottling
to	to	to	to	to	to	to	to	to			
8/26/47	12.0	4,200,000	18,080	59	28	9	48	8,678	Stool neg. 8/8, 8/20, 8/26		+ bronchovascular markings
9/ 3/47	12.0	4,160,000	8,350	3	35	2	10	955	Stool ova neg. 9/3	Hexylresorcinol 0.8 Gm. 9/20/47	Cleared except increased hilar markings
to			to	to	to	to	to	to	Stool ova pos. Ascaris 9/21, Stool neg. 9/30, 10/1, 10/3, 10/8		
10/ 8/47			10,150	39	51	3	17	1,725			
10/16/47			10,050	8	38	1	13	1306	Stool neg. 10/16, 10/21		
to				to							
10/21/47				37							
10/30/47	10.2	3,390,000	6,950	4	23	0	13	504	Stool neg. 10/30, 11/12, 11/25/47		
to	to	to	to	to	to	to	to	to			
12/25/47	12.5	3,650,000	7,950	62	53	1	7	903			

Studies of blood chemistry following this episode are shown in Table III. An electrocardiogram was normal. The paranasal sinuses were normal by examination and by x-ray. Repeated examinations of gastric washings and feces remained negative for acid-fast bacilli. Upon discharge on Dec. 28, 1947, the x-ray of the lungs showed only some residual hilar streaking on the right side; the white blood count was 7,200, with 7 per cent eosinophiles. There was a 12 pound weight gain.

CASE 2.—J. C., Sea View No. 30090, a 19-year-old Negro girl, was transferred from another city hospital to Sea View Hospital on Nov. 15, 1946, with a diagnosis of pulmonary tuberculosis.

Her present illness began in July, 1946, with productive cough, loss of energy, and occasional pain in the left chest. A few weeks later hemoptysis occurred. She was treated at home for asthmatic bronchitis. After three months, she was sent to a hospital where a provisional diagnosis of tuberculosis was made. During the first four months of illness she lost 27 pounds in weight.

Family history and past history were noncontributory, and there was no history of allergy.

Physical Examination.—On admission to Sea View Hospital on Nov. 15, 1946, the patient appeared acutely ill and showed recent weight loss. Her temperature was 101° F.; pulse and respirations were normal. Medium moist râles were heard over the upper two-thirds of both lungs with scattered wheezes. Remainder of the examination was negative.

Laboratory Findings on Admission.—Chest x-ray showed fine mottled exudative densities fanning from the hilum into the adjoining lung field on the right, and similar, though less prominent, densities on the left. The hilar markings were exaggerated. The findings suggested mediastinal lymphadenopathy with parenchymal infiltration. The blood count was 4,900,000 red blood cells, 97 per cent hemoglobin, 6,300 white blood cells with 49 per cent segmented polymorphonuclear leucocytes, 3 per cent nonsegmented cells, 5 per cent eosinophiles, 38 per cent lymphocytes, 4 per cent monocytes, and 1 per cent basophiles. One week later, the white blood cells were 6,450 with 11 per cent eosinophiles. The erythrocyte sedimentation rate was 9 mm. per hour (Westergren). Urine was normal. Mantoux test (1:1,000) was positive. Repeatedly sputa and gastric washings were negative for acid-fast organisms.

Clinical Course.—Two weeks after admission, the chest x-ray showed no change. *Ova of N. americanus were found in the stools.* Eleven days after the administration of hexylresorcinol, the stools became and remained negative for ova. One month after the antihelminthic treatment had been given, the patient showed marked clinical improvement; her lungs and chest x-rays were clear. At discharge in April 1947, six months after admission, the white blood count was 5,300 with a 2 per cent eosinophilia.

CASE 3.—A.W., Bellevue Case No. 55039-47, a 10-year-old Puerto Rican boy, was admitted to Bellevue Hospital on Nov. 25, 1947, complaining of pain in the chest, productive cough, difficulty in breathing after climbing several flights of stairs, for four days. The cough continued and became productive of a yellowish white sputum.

Family history was negative for allergy and tuberculous contact. The patient arrived from Puerto Rico eight months previously. There was no history of allergy or passage of worms.

He was a thin 10-year-old Puerto Rican boy who appeared ill but not in acute respiratory distress. There was marked dental caries. Tonsils were moderately hypertrophied, and the pharynx was slightly injected. Expiratory wheezes and occasional crepitant râles were heard over the right upper chest

anteriorly and the lower chest posteriorly. The liver was palpable below the right costal margin and was slightly tender. The remainder of the examination was negative.

Laboratory findings on admission revealed a hemoglobin of 13.9 Gm. red blood cells 5,400,000 per c.mm., reticulocytes were present, hematocrit 35, white blood cells 32,200 per c.mm., with 12 polymorphonuclear leucocytes, 13 lymphocytes, 1 monocyte, and 73 eosinophiles per 100 white blood cells. The platelets were adequate and red blood cells were of normal morphology. The urine was negative. Nose and throat cultures contained 5 per cent pneumococci and 10 per cent beta hemolytic streptococci. Sedimentation rate was 9 mm. in one hour (Cutter). Blood Mazzini was negative. Tuberculin patch test was positive. Sternal bone marrow done on Nov. 26, 1947, revealed a striking increase in the eosinophilic myelocytes 26 per cent and mature eosinophiles 19 per cent. Erythropoiesis was normal. *No qualitative change in the eosinophiles could be found.*

Fig. 1 (Case 3).—Increased bronchial markings bilaterally and diffuse fine mottling throughout both lung fields.

Roentgenogram of the chest on Nov. 26, 1947, revealed increased bronchial markings and a diffuse fine mottling throughout both lung fields (Fig. 1). Two days later these densities were more definite and confluent. There was accentuation of the left root.

Course.—The additional laboratory studies are shown in Tables III and IV.

Stool specimens revealed *Giardia lamblia and Trichuris trichiura.* A twenty-four-hour stool specimen was negative for schistosoma. Duodenal drainage for strongyloides was negative. After a vermifuge of hexylresorcinol on January 18, the patient passed a single male ascaris. No further worms were passed after two subsequent treatments with hexylresorcinol.

Blood examinations and chest roentgenograms of the parents were negative.

Cough and chest pain disappeared after two days. The patient ran an irregular low-grade fever to 101° F. (rectal). After three weeks, he was afebrile; the lungs were clear. Benadryl 25 mg. t.i.d. had been given for a week without effect.

TABLE III. HEPATIC FUNCTION TESTS IN THREE PATIENTS WITH PROLONGED EOSINOPHILIA AND PULMONARY INFILTRATION

CASE	PROTEIN TOTAL (GM. PER 100 C.C.)	ALBUMIN (GM. PER 100 C.C.)	GLOBULIN (GM. PER 100 C.C.)	CEPHALIN FLOCCULATION	CHOLESTEROL TOTAL	CHOLESTEROL ESTERS	BILIRUBIN	OTHER TESTS	EOSINOPHILIA EXTENT DURATION	COMMENTS
Case 1 admitted 7/15/47								N.P.N., 39.5	Total W.B.C. range from 6,950 to 29,850 with eosinophiles 7-65%	Liver was never palpable Colloidal gold course flat on 9/21
7/16/47	6.28							8/26 Kahn + Wassermann –		
9/ 3/47	10.40	4.98	5.42	++				2 wk. later Kahn – Wassermann +		
10/16/47	8.40	3.76	4.64					2 wk. later Kahn –		
11/25/47	8.00	3.68	4.32							
12/25/47				–						
Case 3 admitted 11/25/47				+ 1/ 8/48 Weakly + 1/14/48				Wassermann –	Total W.B.C. range from 8,100 to 35,000 with eosinophiles of 10-86%	Liver palpable and tender for a time
Case 6 admitted 6/25/49										
7/ 5/49	7.05	3.58	3.47	Weakly +	156	145	0.91	Alkaline phosphatase, 7.77	Total W.B.C. range from 12,600 to 32,000 with eosinophiles of 34-58% for 51 days	Liver 3 cm. below costal margin
7/20/49	7.38	4.3	3.08	+	167	149	0.9	Alkaline phosphatase, 7.2; Brom. sulfophthalein neg. 30 min.		
8/ 8/49	7.0	4.3	2.7	Weakly +	174	128	0.81	Vandenburg delayed		

TABLE IV. STUDY OF BLOOD PICTURE CORRELATED WITH ROENTGENOGRAMS AND INTESTINAL PARASITIC INFECTION (CASE 3)

DATE	HB. GM.	R.B.C.	W.B.C.	POLYS. %	LYMPHS. %	MONO. %	EOSINO. %	TOTAL	X-RAYS	FECES FOR OVA AND PARASITES	TREATMENT FOR OVA AND PARASITES
11/26/47	11.5	5,400,000	26,000	9	12	1	64	16,640	++ 11/26/47		
to	to	to	to	to	to		to	to	to		
12/15/47	13.9	5,800,000	32,350	19	17		79	23,506	++++ 12/ 1/47		
12/22/47	12.5		29,500	12	11	1	62	18,290	++++	1/19/48 one	1/18/48 Hexyl-
to	to		to	to	to	to	to	to	to	male ascaris	resorcinol 0.6
1/14/48	13.9		33,600	20	16	2	77	23,820	+++		Gm.
1/21/48	13.0	5,300,000	22,000	5	9		65	14,300		2/ 1/48 stool	1/29/48 Hexyl-
to	to	to	to	to	to	1	to	to	+++	pos. for trich-	resorcinol 0.8
2/23/48	13.5	5,400,000	35,000	23	13		86	30,100		uris and *G.*	Gm.
										lamblia	
3/ 1/48	12.2		9,500	20	18	4	10	950	+++	3/10/48 stool	3/ 9/48 Hexyl-
to	to	5,200,000	to	to	to	to	to	to	to	neg.	resorcinol 1.0
3/15/48	12.8		18,000	70	32	5	49	8,820	++		Gm.
3/25/48	12.6	4,950,000	8,100	28	11	2	37	3,500	+		
to	to	to	to	to	to	to	to	to	to		
4/22/48	13.1	5,350,000	12,200	42	26	8	44	4,872	++		
5/ 5/48			15,000	15	10	1	64	9,900	+		
to			to	to	to	to	to	to	to		
6/14/48			18,000	19	18	4	69	12,470	++		

The boy remained asymptomatic and clinically well, although the chest roentgenogram was unchanged. On December 1, the densities in both lung fields had become more confluent and the right root was accentuated. There was increased streaking in the base posteriorly in the lateral view. On Jan. 1, 1948, heavy streaking upward and downward from both roots and heavy confluent densities were seen bilaterally. On January 26, the dense infiltration noted had cleared somewhat leaving a residual fine mottling. The position, size, and character of the pulmonary infiltrations had changed from time to time in this two-month period, but there was little quantitative difference from the roentgenographic appearance on admission (Table IV).

During these two months no significant hematologic change was observed. The total white blood cell count remained about 30,000 cells per c.mm. The total number of eosinophiles remained between 20,000 and 25,000 per c.mm., and the polymorphonuclear leucocytes were consistently about 5,000 per c.mm. In Table IV it is significant that the changing total of white blood cells reflects the change only in the number of eosinophiles since the polymorphonuclear leucocytes maintain a plateau. Coincident with the passage of a male ascaris on January 18 was a slight drop in the total number of both the white blood cells and the eosinophiles.

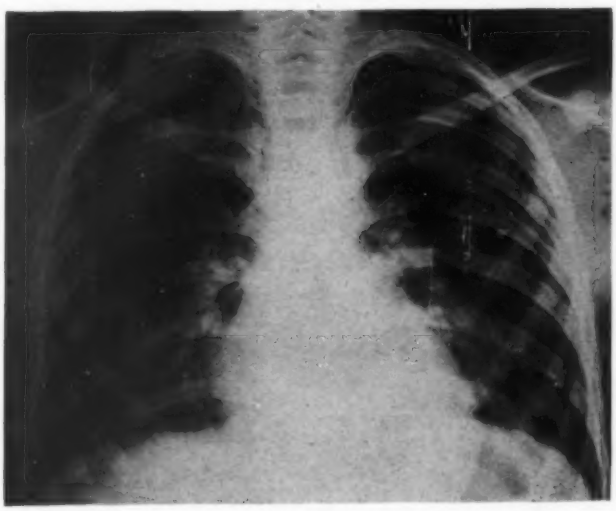

Fig. 2 (Case 3).—Few scattered nodular infiltrations, greater in left lung, six months after Fig. 1.

The patient remained well until discharge. His eosinophilia showed little change except for one period (see Table IV). On April 22, a sternal bone marrow revealed an abundance of cells of the eosinophilic series with 28.9 per cent mature cells, and 5.5 per cent eosinophilic myelocytes.

The pulmonary infiltration cleared almost completely for the first time on March 25, four months after admission to the hospital. One month later there was a recurrence with a diffuse fine mottling throughout both lung fields which gradually cleared. The last films taken on June 15 showed only a few scattered nodular infiltrations, greater in the left lung (Fig. 2).

When last seen there was still an eosinophilia and an increased total white blood cell count. In June the parents took the patient to Puerto Rico and no further reports are available.

Familial eosinophilia[46] was excluded by the negative findings on both parents. It is difficult to know which one of the intestinal parasites found in this patient is the most likely provocative allergic agent. Trichinosis[23] may present a similar picture. Despite the positive skin test, the low titer of the precipitin test 1:370 makes trichinosis a tenuous diagnosis. Trichuriasis is rarely associated with an eosinophilia of such proportion. Ascariasis, with hypersensitivity to the ascaris antigen, seems the most likely possibility. Marked eosinophilia has been repeatedly associated with this intestinal infestation.

CASE 4.—J. C., Bellevue Case No. 4045-49, a Puerto Rican boy 4 years of age, was admitted to Bellevue Hospital on March 15, 1949, from the out-patient department. When he came to New York City from Puerto Rico in July, 1948, he was very weak and listless. He had an almost constant diarrhea of five to six loose stools daily containing occasional pus and blood, from July, 1948, until he was seen in the outpatient department at Bellevue in February, 1949, where stool examinations disclosed ova of ancylostoma, ascaris, and trichuris, and a chest x-ray showed diffuse infiltration in both right and left bases, although the lungs were clear. There was an eosinophilia of 10 per cent with a hemoglobin of 8.29 Gm. and a white blood cell count of 14,000.

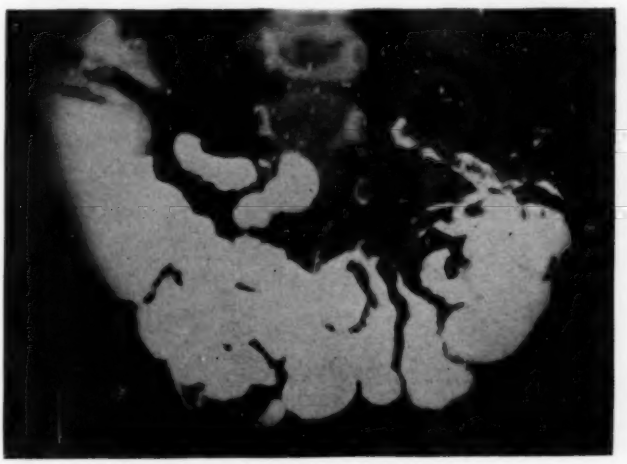

Fig. 3 (Case 4).—Ascarids outlined in small bowel.

In the hospital the boy appeared pale, malnourished, but alert and not acutely ill. There was evidence of recent weight loss. The lungs were clear; the liver was not felt; a low-pitched soft systolic murmur was heard along the sternal border. There was no cardiac enlargement.

Family history and personal history were negative for tuberculosis and allergy. A Mantoux test was negative to 1 mg. of old tuberculin. Stool specimen again showed ova for ancylostoma, trichuris, and ascaris; in addition *G. lamblia* and *E. nana* cysts were found. Serial x-ray studies of the gastrointestinal tract using barium surprisingly disclosed several ascarids clearly outlined in the small bowel (Fig. 3). The eosinophilia during this eighteen-day hospital stay ranged

from 2 to 10 per cent, the white blood cell count from 16 to 29,000, and the hemoglobin averaged about 10 Gm. A roentgenogram of the chest taken on April 11, 1949, showed some clearing, but there was still perihilar infiltration in the right lung with fibrosis at the base.

Hexylresorcinol 0.3 Gm. was given twice a day at four-day intervals for two courses of treatment and two ascarids were passed. On April 1, Atabrine 50 mg. was given twice daily for the giardia infection. A week later, the patient appeared well, the stools were negative for parasites, the lungs were still clear, and there was no eosinophilia.

CASE 5.—V.C., Bellevue Case No. 200-49, a Puerto Rican boy 8 years of age, was admitted to Bellevue Hospital on Jan. 1, 1949. He had been well until Nov. 15, 1948, when he began to have some fever, a cough productive of clear sputum, fatigue, anorexia, and a moderate weight loss. He had been treated in another hospital because he coughed up "one-half cup of bright red blood" a few hours before admission. The patient came from Puerto Rico three years previously. No history of allergy was obtained. A sister, 14 years of age, had been under observation for possible tuberculosis. The family, including the patient, were negative by x-ray and Mantoux tests done six months before this admission.

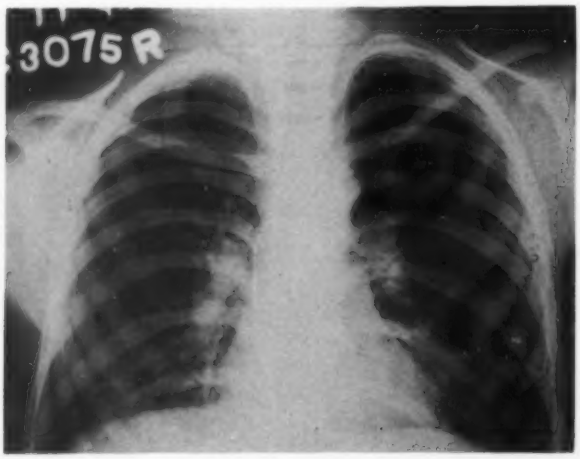

Fig. 4 (Case 5).—Prominent root infiltration more marked on the right, with heavy streaking extending to the bases. The streaking on the right side extends outward into the eighth posterior interspace.

The boy was emaciated, weighing only 40 pounds, and was very small for his age. He was acutely ill and showed recent weight loss. There was general glandular adenopathy and an injected pharynx. Many inspiratory wheezes were heard throughout the chest. On first examination the hemoglobin was 8 Gm. The total white blood cell count was 9,000 with a differential count of 59 per cent polymorphonuclear neutrophiles, 15 per cent eosinophiles, 13 per cent lymphocytes, and 7 per cent monocytes. Two days later the eosinophiles had dropped to 2 per cent and remained at normal levels throughout the observed three weeks. The Mantoux test was negative to 1 mg. of old tuberculin. Mazzini test and urine examinations were also negative. Cultures of gastric washings for *Myco. tuberculosis* were negative. Roentgenogram of the lungs on admission showed extensive hilar streaking bilaterally which cleared within a week. Pneumococci

(not typed) and hemolytic *Staphylococcus aureus* were cultured from the nose and throat.

The bronchopneumonia was associated with a temperature of 100° to 104° F. (rectal) for several days, some cough, headache, abdominal pain, and occasional blood-tinged loose stools. Sulfadiazine and penicillin were given for four days. In a few days the lungs were clear by physical examination and roentgenogram.

Stool examinations were guaiac-positive and ova identified as ancylostoma and trichuris were found. Tetrachloroethylene was given, together with Feosol for his anemia. On January 21, the hemoglobin had risen to 12.5 Gm., and the stools were free of parasites. He was well and the chest was clear on Jan. 23, 1949, when he was discharged.

CASE 6.—N.R., Bellevue Case No. 50557-49, a 12-year-old Puerto Rican boy, was referred to Bellevue Hospital on June 25, 1949, because of hepatomegaly discovered in the course of a routine physical examination at school. There were no complaints nor symptoms.

Past history and family history were noncontributory. No history of allergy nor tuberculosis was obtained.

He was a thin boy who did not appear ill. His lungs were clear on admission. A soft systolic murmur was heard along the left sternal border but there was no cardiac enlargement. The sharp edges of the liver could be easily felt 3 cm. below the costal margin.

Two days after admission an eosinophilia of 42 per cent was found with a leucocytosis of 17,400. Tuberculin patch test done June 27 was positive. Skin tests for trichinella were negative in dilutions of 1:5,000. On July 7, ova of *S. mansoni, E. coli, E. nana,* ancylostoma, and trichuris were found. Later ova for strongyloides were also discovered.

In view of the hepatomegaly, liver function tests were done. The results are indicated in Table III.

The patient was never very ill but on July 20, more than three weeks after admission, he developed a slight fever and crackling râles. Chest roentgenograms showed an increasing shadow in the right base interpreted as a pneumonitis of the posterior basal segment of the right lower lobe. The râles in the chest cleared within three days, and the pulmonary shadow cleared in two weeks. In all x-rays calcification in the right root was seen, most likely a residua of an old tuberculous infection. Throughout the hospital stay repeated white blood cell counts ranged from 12,600 to 32,000 and the eosinophiles from 34 to 58 per cent.

The therapy consisted of tetrachloroethylene 1.5 c.c. twice daily at five-day intervals for hookworm, followed later by a second and third course using a dosage of 2 c.c.; gentian violet 50 mg. three times daily for seven days for strongyloides; Fuadin 2 c.c. intramuscularly daily for twenty days for schistosoma, and chloraquin for five days for giardia infection.

On August 30, only the ova for strongyloides and trichiuris could be found in the stool. On September 1, the patient was discharged to be followed in the out-patient department.

CASE 7.—J.Q., Bellevue Case No. 44900-49, a 7-year-old Puerto Rican girl, was admitted to Bellevue Hospital on Dec. 7, 1949, with periumbilical pain, and vomiting for twelve hours. She had been previously well. The night before admission she passed a worm in the stool. She was a malnourished girl, not actuely ill, but she had R.L.Q. and rectal tenderness, some spasticity and a questionable mass in the R.L.Q. The remainder of the physical examination was negative.

Other findings on admission were temperature of 100.6° F., pulse 120, respiratory rate 26, negative urinary findings, erythrocyte sedimentation rate of 9 mm. per hour, and a white blood cell count of 14,000 with 70 per cent polymorphonuclear cells and no eosinophiles. Tuberculin patch and Mazzini tests were negative.

An appendectomy was done on December 7. Although the appendix was normal, the serosa of the terminal ileum was injected, edematous, and contained a large firm mass, presumably *A. lumbricoides*. The microscopic cross section of the appendix showed numerous intestinal parasites, thought to be *T. trichiura*.

The postoperative course was uneventful. On December 12 and again on December 31, Crystoids of hexylresorcinol, 1.0 Gm, were given. Numerous worms and ova were passed which were identified as *T. trichiura* and *A. lumbricoides*.

Within twenty-four hours (January 1) the patient developed a mild cough without other symptoms except slight elevation of temperature. On Jan. 4, 1950, numerous coarse and medium moist râles and wheezes were heard in both lung fields. These physical signs cleared within a week. Throughout this time, the patient was not ill; she had occasional, slight fever, and an infrequent dry cough.

Fig. 5 (Case 7).—Bilateral hilar streaking to the bases, greater on the right side, and a small amount of fluid obliterating the left costophrenic angle.

On January 5, the chest x-ray revealed bilateral hilar streaking to the bases, greater on the right side, and a small amount of fluid obliterating the left costophrenic angle (Fig. 5). The findings were not present in an x-ray taken Dec. 28, 1949 (a flat film of the abdomen which also visualized most of the chest). On January 6, the nose and throat cultures contained influenza-like organisms, and a pneumococcus. The rise in eosinophile count with this picture is significant and given below.

White Blood Cells

	Total Per C.Mm.	Polymorphonuclear Per Cent	Eosinophile Per Cent
12/ 7/49	14,000	70	0
1/ 6/50	10,450	44	8
1/ 9/50	14,250	60	16
1/20/50	13,700	53	9

The patient was asymptomatic on January 19, and the chest was clear by physical examination and by x-ray. Two days late she was discharged.

CASE 8.—A.M., Bellevue Case No. 46226-49, an 11-year-old girl, was admitted to Bellevue Hospital on Dec. 29, 1949, because of cough and fever for five weeks since her arrival from Puerto Rico. The cough was productive of yellowish sputum, the fever had been irregular and increasingly higher, and the patient had been complaining of restlessness and fatigue. In previous examinations in the out-patient department a tuberculin patch test was negative, the stools contained no parasites nor ova, but a blood eosinophilia of 25 per cent was found. Findings in the lung x-rays suggested a possible tuberculous infection. There was a patch of consolidation in the first right interspace with a small highlight in this area suggesting cavity formation.

The past history was noncontributory except for a diagnosis of worm infestation in Puerto Rico seven years previously and a history of contact with a paternal uncle ill with tuberculosis.

On admission to the hospital, the patient did not appear ill although she was coughing frequently, and the temperature was 100.2° F., the pulse 104, and the respiration 24. There was slight puffiness about the eyes. Dullness and diminished breathing were found over the right upper lobe anteriorly. Much lymphoid tissue was seen in the posterior pharynx. The nasal turbinates were moderately enlarged.

The patient improved rapidly; the temperature was normal within twelve hours, and the cough and abnormal findings in the lungs cleared within a week.

Trichinella skin test was negative on December 30, and several stool examinations revealed no ova nor parasites even after hexylresorcinol and purgatives were given. Cephalin flocculation test was strongly positive on Jan. 3, 1950.

Marked clouding of the ethymoid and maxillary cells was seen in the x-ray. On admission (Dec. 29, 1949), the x-ray of the lungs was similar to that taken two days previously in the out-patient department. The pulmonary fields were entirely clear on January 3.

Gastric washings of January 9 and 10 were negative on culture for *Myco. tuberculosis.*

An eosinophilia was present throughout the hospital stay varying from 18 to 33 per cent with total white blood cell counts of 7,100 to 13,800.

The patient received the Proetz treatment on two occasions for her sinusitis, particularly the right antrum. After the first week she was symptomatically well and the erythrocyte sedimentation rate had fallen from 32 mm. in one hour (Cutler method) on admission, to 19 on January 17. Although the eosinophilia remained high, the patient was discharged from the hospital on January 24 to be followed in the out-patient department.

DISCUSSION

The eight patients presented here illustrate the varied clinical picture associated with Loeffler's syndrome. The last five patients fit the original description. Each had a short, benign course, with x-ray shadows which cleared in seven to eighteen days. The symptoms were mild. In one patient (Case 6) there were no respiratory symptoms. The eosinophilia in this instance directed the search for pulmonary infiltration. Careful examination revealed a small area with resonant râles which persisted for only two days. The x-ray shadow remained for two weeks. The physical signs of pulmonary disease were transient in Patients 5, 6, 7, and 8 where râles and wheezes were heard for only a few days, while in

Patient 4 no physical signs were heard at any time. Since this patient was ambulatory and examined only at weekly intervals, protean signs may have been missed.

By contrast, the first three patients described here illustrate chronicity of Loeffler's syndrome. Fine mottling throughout the lung fields simulating miliary tuberculosis was seen in the x-rays in these three patients. In Cases 1 and 3, the shadows persisted for seven and one-half months and in Case 2 for seven weeks.

The physical signs were never striking and consisted chiefly of scattered resonant râles which were variable and cleared early in two patients, but in Case 1 they persisted nine months. Persistent and constant was the eosinophilia which often remained after the x-ray shadows had disappeared.[44]

The symptomatology was variable. Some patients showed frank symptoms of pulmonary disease such as cough, expectoration, and fever. Others were symptom-free even though the involvement of the lung was evident by physical signs. In Cases 4 and 6 diarrhea and hepatomegaly were the presenting problems.

In some patients, liver function tests were done because of hepatomegaly. Liver damage was discovered in three patients (the disturbance of function was present during the active phase of the disease and cleared during convalescence) (see Table III). It may be significant that these three patients had the most sustained and markedly elevated eosinophilia. The size of the liver alone cannot be a guide to disturbed function as exemplified in Case 1, where the liver was never palpated.

The most likely provocative allergen in the first seven patients herein described was an intestinal parasite despite the fact that four of these children had positive skin tests for tuberculosis. In all four, no positive cultures for *Myco. tuberculosis* could be obtained on repeated attempts. Moreover, the clinical course and physical signs were not those of miliary tuberculosis, and the eosinophilia in three of these (Cases 1, 3, 6) was much greater than that usually found in tuberculosis. The improvement following treatment for the intestinal parasite makes the differential etiological diagnosis clear. Relapses in Patients 1 and 6 were associated with the recurrent finding of ova in the stools when the examination had previously been negative, suggesting an increase in allergen from the intestinal parasite as the infestation again became apparent.

The importance of differentiating tuberculous pulmonary infection from Loeffler's syndrome is indicated in Cases 1, 2, and 3. These patients were kept for weeks on tuberculosis wards until the diagnosis was clarified. In those patients with miliary mottling, the differential diagnosis between Loeffler's syndrome and tuberculosis is difficult. In favor of the Loeffler's syndrome are the following: the well-being of the patient, the absence of splenomegaly, absence of other evidence of tuberculous miliary spread, marked and persistent eosinophilia, and the negative cultures for *Myco. tuberculosis*.

An allergic background was found in only one patient but since some of these patients were from Puerto Rico and had been separated from the parents

who gave the history, the stories are not reliable. The allergic pattern in the lung is suggested by the finding of "wheezes" bilaterally in three patients (Cases 3, 5, and 7). Moreover, a diagnosis of asthma by symptomatology and examination of the lungs was made in two other patients in medical centers elsewhere (Cases 1 and 2).

Pleural exudate may occur in Loeffler's syndrome. Bayley and collaborators[26] reported a case with free pleural fluid found at autopsy. Recent experimental work by Loeffler, Essellier, and Macedo[47] with ascaris infestation in guinea pigs indicated the presence of pleurisy. They found pleural irritation when an ascaris or larvae was immediately in contact with the pleura. Direct pleural irritation by the parasite must be seriously entertained in Case 7 where there was a heavy infestation with ascaris and trichuris (appendectomy disclosed trichuris in cecum and appendix).

Harkavy's[11] emphasis on the role of bacterial allergy, particularly from infections in the upper respiratory tract in the Loeffler's syndrome, may be applied to the interpretation of Case 8. In this patient no etiological agent could be found except the infected ethmoid and maxillary sinuses. Although eosinophiles in the smears of the nasal secretions never exceeded 20 per cent, bacterial allergy with eosinophilic allergic reaction in the lungs is not precluded by this finding alone. The patient's pulmonary lesions subsided quickly and coincidentally while the sinus infection was being treated.

The transitory character of some of the pulmonary x-ray shadows may be explained on the basis of atelectasis. Loeffler and co-workers[47] in their experimental work found plugs of mucus and eosinophilic material within the bronchi, and in other instances larvae of ascaris were found occluding the bronchi. Sharply demarcated areas of atelectasis of differing sizes were described adjoining these bronchi. Eichwald and Singletary[48] suggest that the x-ray lesions are allergic and comparable to the "id" reaction described by the dermatologist. They offer the term "pneumonid" to describe the pulmonary process seen in the Loeffler's syndrome.

It should be emphasized that Loeffler's syndrome is not necessarily a benign disease in terms of duration, nor in terms of effect on the total health of the patient. The loss of weight or failure to gain in some patients is significant, and the impairment of liver function may further interfere with the health of the patient. More study relative to this disturbed physiology should be done.

Experimental, pathologic, and clinical evidence clearly indicates that Loeffler's syndrome is an allergic manifestation in which the most apparent and the major shock organ is the lungs. In all instances search for the provocative agent of the allergy is essential.

Although multiple etiological agents have been described with this syndrome, no constant clinical nor roentgen picture can be associated with any single agent.

SUMMARY

1. Eight patients with pulmonary infiltrations and eosinophilia are described.

2. Five of the cases were mild and corresponded to the original description of Loeffler's syndrome. Three cases were chronic and the condition persisted for months. These cases correspond to the broader and more recent concept of Loeffler's syndrome.

3. Three patients were for a time mistakenly diagnosed as miliary tuberculosis because of the nature of the x-ray shadows and the presence of a positive tuberculin skin test. The importance of differentiating Loeffler's syndrome in patients with positive tuberculin is emphasized.

4. Disturbed liver function was found in the three patients with a chronic course.

5. In seven instances the pulmonary x-ray shadow cleared before the eosinophile count in the peripheral blood returned to normal levels.

6. All of the patients survived. In seven patients intestinal parasitism was found. In the eighth patient, bacterial allergy associated with infected sinuses is suggested as the cause of the Loeffler's syndrome.

REFERENCES

1. Loeffler, W.: Zur Differential Diagnose der Lungeninfiltrierungen; über flüctige Succedan-Infiltrate (mit Eosinophilie), Beitr. z. Klin. d. Tuberk. **79**: 368, 1932.
2. Loeffler, W.: Die flüchtigen Lungeninfiltrate mit Eosinophilie, Schweiz, med. Wchnschr. **66**: 1069, 1936.
3. Kartagener, M.: Chronic Pulmonary Infiltration With Eosinophilia, Schweiz. med. Wchnschr. **72**: 862, 1942. (Abst. J. A. M. A. **121**: 893, 1943.)
4. Alpher, I. M.: Loeffler's Syndrome. Report of Two Cases, One With Recurrent Features, and One Associated With Hay Fever, J. Allergy **18**: 39, 1947.
5. Engel, D.: Ueber eine eigenartige anaphylaktische Erkrankung der Lunge, Beitr. z. Klin. d. Tuberk. **87**: 239, 1936 (cited by Söderling).
6. Meyer, H. E.: Zur Kenntniss flüchtiger mit Eosinophile im Blut einhergehender Lungeninfiltrate, Med. Welt. **11**: 1808, 1937.
7. Söderling, B.: Transient Lung Consolidation, Arch. Dis. Child. **14**: 22, 1939.
8. Hansen-Pruss, O. C., and Goodman, E. G.: Transitory Pulmonary Lesions With Eosinophilia in Asthmatics, Ann. Allergy **2**: 85, 1944.
9. Hansson, N.: Transitory Lung Infiltrations With Eosinophilia, Acta Radiol. **18**: 207, 1937.
10. Smith, D. C. W., and Alexander, A. J.: Loeffler's Syndrome, South. M. J. **32**: 267, 1939.
11. Harkavy, J.: Vascular Allergy: Pathogenesis of Bronchial Asthma With Recurrent Pulmonary Infiltrations and Eosinophilic Polyserositis, Arch. Int. Med. **67**: 709, 1941. Harkavy, J.: Vascular Allergy, J. Allergy **14**: 507, 1943.
12. Maier, C.: Das flüchtige eosinophile Lungeninfiltrat; zusammenfassende Ergebnisse von über 100 Beobachtungen, Helvet. med. acta. **10**: 95, 1943. (Abst.: J. A. M. A. **123**: 869, 1943.)
13. Frimodt-Möller, C., and Barton, R. M.: A Pseudotuberculous Condition Associated With Eosinophilia, Indian M. Gaz. **75**: 607, 1940. (Abst.: Am. Rev. Tuberc. **45**: Jan.-June, 1942.)
14. Weingarten, R. J.: Tropical Eosinophilia, Lancet **1**: 103, 1943.
15. Hodes, P. J., and Wood, F. C.: Eosinophilic Lung (Tropical Eosinophilia), Am. J. M. Sc. **210**: 288, 1945.
16. Apley, J., and Grant, G. H.: Eosinophilia With Pulmonary Disease on Return From the Tropics, Lancet **2**: 308, 1944; **1**: 812, 1945.
17. Soysa, E., and Jayawardena, M.: Pulmonary Acariasis. A Possible Cause of Asthma, Brit. M. J. **1**: Jan., 1945.
Carter, H. F., Wedd, G., and D'Abrera, V. St. E.: Occurrence of Mites (Acarina) in Human Sputum, Indian M. Gaz. **79**: 163, 1944.
18. Wild, O., and Loertscher, M.: Zur Aetiologie der flüchtigen Lungen-Infiltrierungen, Schweiz. med. Wchnschr. **64**: 829, 1934.
19. Koino: Experiment of, cited in Transitory Pulmonary Infiltrations Associated With Eosinophilia, Loeffler's Syndrome, An Editorial, J. A. M. A. **126**: 837, 1944.
20. Beck, L. C.: Loeffler's Syndrome. Report of a Case, Hawaii M. J. **1**: 361, 1942.
21. Venzant Quintana, E.: Infiltrado de Loeffler, provocado por el Necator Americano, Rev. méd-quir. de Oriente **3**: 159, 1942.

22. Wright, D. O., and Gold, E. M.: Loeffler's Syndrome Associated With Creeping Eruption, J. A. M. A. **128**: 1082, 1945.
23. Slowey, J. F.: A Case of Transient Successive Pulmonary Infiltrations Associated With Trichiniasis, Ann. Int. Med. **21**: 130, 1944.
24. Grayce, I.: Pulmonary Infiltrations Associated With Blood Eosinophilia, Clin. Proc. Cape Town Post-Graduate Med. A. **5**: 195, 1946.
25. Hoff, A., and Hicks, H. M.: Transient Pulmonary Infiltrations. A Case of Eosinophilia (Loeffler's Syndrome) Associated With Amoebiasis, Am. Rev. Tuberc. **45**: 194, 1942.
26. Stefano, J.: Sindrome asmático por amebiasis pulmonar, Semana méd. **2**: 749, 1939.
27. Whitehouse, F. R.: Massive Eosinophilia in Ucinariasis: Report of Two Cases, Gastroenterology **9**: 303, 1947.
28. Karan, A. A., and Singer, E.: Transitory Pulmonary Infiltrations Mistaken for Tuberculosis With a Report of 5 Cases, Ann. Int. Med. **17**: 106, 1942.
29. Pirkel, H. B., and Davin, J. R.: Loeffler's Syndrome, Transient Pulmonary Infiltrations With Eosinophilia, Am. Rev. Tuberc. **50**: 48, 1944.
30. Rich, A. R.: Role of Hypersensitivity in Periarteritis Nodosa as Indicated by 7 Cases Developing During Serum Sickness and Sulfonamide Therapy, Bull. Johns Hopkins Hosp. **71**: 123, 1942.
31. Müller, R. W.: Deutsch. med. Wchnschr. **64**: 1286, 1938.
32. Henderson, A. T., and Peirce, C. B.: Transitory Focal Pulmonary Edema and Eosinophilia, Am. J. Roentgenol. **58**: 391, 1947.
33. Willett, F. M., and Oppenheim, E.: Pulmonary Infiltrations With Associated Eosinophilia, Am. J. M. Sc. **212**: 608, 1946.
34. Elsom, K. A., and Ingelfinger, F. J.: Eosinophilia and Pneumonitis in Chronic Brucellosis. A Report of 2 Cases, Ann. Int. Med. **16**: 995, 1942.
35. von Meyenburg, H.: Eosinophilic Pulmonary Infiltration: Pathological Anatomy and Pathogenesis, Schweiz. med. Wchnschr. **72**: 809, 1942. (Abst.: J. A. M. A. **121**: 626, 1943.)
36. Bayley, E. C., Lindberg, D. O. N., and Baggenstoss, A. H.: Loeffler's Syndrome. Report of a Case With Pathologic Examination of the Lungs, Arch. Path. **40**: 376, 1945.
37. Cole and Korns: Cited in Allergy, on Loeffler's Syndrome, Urbach, 1943.
38. Perlingiero, J. G., and György, P.: Chronic Eosinophilia, Report of Case With Necrosis of Liver, Pulmonary Infiltrations, Anemia and Ascaris Infestation, Am. J. Dis. Child. **73**: 34, 1947.
39. Rich, A. R., and Gregory, J. E.: On the Anaphylactic Nature of Rheumatic Pneumonitis, Bull. Johns Hopkins Hosp. **62**: 65, 1943.
40. Pujol, Alfredo, Jr.: Loeffler's Syndrome, An. paulist de med. e cir **52**: 321, 1946.
41. Viersma, H. J.: Syndrome of Löffler: Transitory Pulmonary Shadows and Eosinophilia, Nederl. tijdschr. v. geneesk. **82**: 5372, 1938.
42. Keller, A. E., Hillstrom, H. T., and Gass, R. S.: Lungs of Children With Ascaris, Roentgenologic Study, J. A. M. A. **99**: 1249, 1932.
43. Baer, A.: Report of Case of Transient Pulmonary Edema, Ohio State M. J. **37**: 960, 1941.
44. Stahel, R.: Sternal Befunde bei eosinophilem Lungeninfiltrat, Folia hemat. **59**: 341, 1938.
45. Zuelzer, Wolf W., and Apt, Leonard: Disseminated Visceral Lesions Associated With Extreme Eosinophilia: Pathologic and Clinical Observations on a Syndrome of Young Children, Am. J. Dis. Child. **78**: Aug., 1949.
46. Atmar, R. C.: Familial Eosinophilia; Report of Case With Biopsy of Liver, J. A. M. A. **115**: 449, 1940.
47. Loeffler, W., Essellier, A. F., and Macedo, M. E.: Zur Pathogenese und Aetiologie der flüchtigen Lungeninfiltrate mit Bluteosinophilie (Löffler'sches Syndrom), Helvet. med. acta **15**: 223, 1948.
48. Eichwald, M., and Singletary, W. V.: Transient Successive Pulmonary Infiltrations (Löffler's Syndrome) Radiology **46**: 258, 1946.
49. Holt and McIntosh: Holt's Diseases of Infancy and Childhood, ed. 11, New York, 1939, D. Appleton-Century Co., p. 537.

THE TREATMENT OF SCARLET FEVER WITH PENICILLIN G ADMINISTERED ORALLY THREE TIMES A DAY

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THE efficacy of penicillin administered by the oral route in the treatment of infections due to organisms of a high order of sensitivity to this agent has been proved beyond any doubt by a number of investigators.[1-21, 23-29] Although this drug is partially destroyed in the gastrointestinal tract, good clinical results are obtainable if attention is paid to the time of administration with respect to food intake and if about four to five times the effective parenteral dose is given. In spite of the fact that frequent intramuscular injection of crystalline penicillin G produces a remarkable shortening of the acute phase and reduction in the incidence of suppurative complications in streptococcal pharyngitis and scarlet fever, this method of therapy is generally impractical except in the hospital. Repository forms of penicillin, for example the procaine salt, are effective in acute streptococcic disease of the upper respiratory tract, but even this form of treatment leaves a lot to be desired since it still requires the daily attendance of a physician or nurse and does not eliminate completely the pain and psychic trauma connected with an injection. For these reasons, penicillin has been given by mouth to patients with infections produced by the beta-hemolytic streptococcus and results approximating those produced by parenteral administration obtained.

The purpose of the work reported in this paper was fourfold: (1) to compare the effectiveness of various quantities of penicillin administered orally on the clinical and bacteriologic course of scarlet fever; (2) to ascertain the smallest oral dose of the drug which is effective in scarlet fever; (3) to give the antibiotic agent only every eight hours for ten days in order to evaluate so-called "discontinuous" therapy; (4) to determine blood levels of penicillin in patients treated by this method.

METHODS

Every patient with scarlet fever admitted to the Haynes Memorial Hospital was treated with penicillin if the duration of the infection was less than forty-eight hours and no antibacterial therapy had been given prior to admission. An attempt was made to grade the severity of the disease at the time of entry to the hospital on the following bases: *Severe*—temperature over 103° F., white blood count higher than 15,000, widespread rash with petechial and/or vesicular components, complaint of severe discomfort in the throat, marked edema, red-

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ness, exudate, and hypertrophy of the lymphoid tissue in the pharynx, and symptoms of severe toxicity such as headache, nausea, vomiting, and pains in the joints or muscles. *Moderate*—temperature between 101 and 103° F., white blood count ranging from 10,000 to 15,000 cells per cubic millimeter, rash developing in typical fashion but not very bright and without petechiae, only moderate difficulty in swallowing, redness and edema of the pharyngeal tissues without exudate, and only slight or no symptoms suggesting toxicity. *Mild*—temperature below 101° F., normal white blood count, rash quite sparse and light in color, minimal pharyngeal discomfort, mild to moderate redness of the pharynx without edema or exudate and no symptoms of toxicity; in most of these cases the rash disappeared in twenty-four hours or less.

Throat and nose cultures were made at the time of admission and daily thereafter by means of sterile cotton swabs which were streaked on blood-heart infusion-tryptose-yeast agar and seeded at the same time into broth of the same composition. As many of the strains as possible were later examined serologically for the type of group specific polysaccharide and type-specific nucleoprotein M. Complete physical examinations were carried out daily; all temperatures were taken rectally every four hours. White blood counts were made at least twice a week, urine examinations at least three times weekly, and sedimentation rates (Westergren) determined once a week during the entire period of residence in the hospitals. Electrocardiograms were not taken routinely but were made in all instances where a clinical suspicion of rheumatic fever was present. Changes in the appearance of the rash were followed carefully and the time of disappearance of the exanthem as well as beginning of desquamation noted. The pharynx of each patient was examined daily and the degree of lymphoid hyperplasia, redness, exudate if present, tonsillar enlargement, and difficulty in swallowing noted. The time of disappearance of such toxic manifestations as arthralgia, headache, nausea, vomiting, and diarrhea were determined.

Practically all of the patients were detained in the hospital for a minimum period of three weeks, while those who developed a complication or showed any abnormality in the course of their disease were held for a longer period of time. Follow-up studies were not carried out except in those instances in which a suspicion of the presence of rheumatic fever or glomerular nephritis had been present during the period of hospitalization.

The penicillin preparation employed was crystalline G compounded in a tablet containing 100,000 units and calcium carbonate. The drug was administered every eight hours; it was always given not later than one-half hour before or earlier than two and one-half hours after a meal; for the younger patients the pills were broken into small pieces in order to facilitate swallowing. Varying doses of antibiotic agent were used in this study.

The penicillin dosage schedules employed were as follows: (1) 100,000 units of crystalline penicillin G intramuscularly every eight hours; this group served as controls for those who received the medication by mouth; (2) 800,000 units orally every eight hours; (3) 500,000 units orally every eight hours; (4) 300,000 units orally every eight hours; (5) 150,000 units orally every eight hours in

the usual tablet to which had been added a flavoring material; (6) 150,000 units orally every eight hours of unflavored penicillin; (7) 100,000 units orally every eight hours; and (8) 50,000 units orally every eight hours.

All patients who were free of beta-hemolytic streptococci in the respiratory tract for at least three days while receiving penicillin were transferred to "clean" wards, where no fresh cases of scarlet fever were admitted, for the completion of treatment and observation in order to avoid cross infection with streptococci.

Determinations of blood concentrations of penicillin were made in most of the cases on the second and ninth days of therapy. Blood was drawn at varying intervals following the administration of the morning dose and the quantity of antibiotic assayed by the method of Rammelkamp.[22] Only the plasma levels present on the second day of treatment are discussed in detail below.

RESULTS

A total of 356 patients was studied; of these 154 were between the ages of 2 and 8 years, 161 ranged between 8 and 14 years, and 41 were over 15 years of age. The sexes were about evenly divided. Classification of the cases on the basis of severity of the scarlet fever showed 9 with severe, 294 with moderately severe, and 53 with mild disease. Forty-one per cent had had a sore throat for less than 24 hours and 72 per cent for less than 48 hours before institution of treatment.

Time Required for the Temperature to Return to Normal.—The administration of 100,000 or 150,000 units of penicillin orally every eight hours produced complete defervescence in 82 to 85 per cent of the patients within seventy-two hours. The smallest number of patients reaching a normal temperature level in seventy-two hours, 70 per cent, was observed when a dose of 100,000 units of antibiotic was given intramuscularly every eight hours. From the detailed data presented in Table I it would appear that the quantity of penicillin most effective in producing rapid defervescence was 100,000 or 150,000 units orally.

Time Required for Pharyngitis to Disappear.—Disappearance of discomfort in the throat and of visible evidence of pharyngeal infection was quite rapid with oral therapy. From 70 to 80 per cent of the patients had no evidence of streptococcal pharyngitis within seventy-two hours after initiation of therapy. The best results were obtained with 300,000 units of penicillin given orally. The rapidity of healing was not greater when 100,000 units of drug were administered intramuscularly. The data pertaining to the rate of disappearance of subjective and objective evidence of upper respiratory tract infection are presented in Table I.

Time Required for the Peripheral White Blood Count to Return to Normal.—The administration of penicillin by mouth resulted in a much more rapid return of the peripheral white blood count to normal than is usually observed in patients with scarlet fever not receiving specific antibacterial agents. As can be seen in Table I, the majority of patients in each dosage group had a normal number of circulating leucocytes at the end of one week of therapy. That

parenteral administration of the drug did not produce better results is suggested by the fact that 65.2 per cent of the patients receiving 100,000 units of penicillin by mouth every eight hours had normal white blood count within one week whereas the same was true in only 56.2 per cent of those given the same quantity of antibiotic agent at the same interval intramuscularly. The effect on the leucocyte count produced by the eight-hour schedule of oral therapy was no less marked than that observed previously with the use of 15,000 units of penicillin intramuscularly every three hours.[30, 31]

Time Required for the Sedimentation Rate to Return to Normal.—In patients with scarlet fever who are treated "symptomatically" the sedimentation rate does not return to normal usually until late in the third week of the disease.[31] When 15,000 units of penicillin are given intramuscularly every three hours most patients have normal sedimentation rates sometime during the second week.[31] As can be seen from Table I, the sedimentation rates in the vast majority of patients who were treated by the oral route only every eight hours returned to normal levels within fourteen days after the initiation of therapy. The administration of 100,000 units of penicillin by mouth three times a day seemed to be more effective in lowering the sedimentation rate than the same quantity of drug given intramuscularly.

TABLE I. EFFECT OF VARIOUS PENICILLIN DOSAGE SCHEDULES ON SOME CLINICAL AND LABORATORY FEATURES OF SCARLET FEVER

DOSE OF PENICILLIN GIVEN EVERY 8 HOURS, AND ROUTE OF ADMINISTRATION	PER CENT OF PATIENTS WITH TEMPERATURES NORMAL ON THIRD DAY OF TREATMENT	PER CENT OF PATIENTS IN WHOM SORE THROAT DISAPPEARED AFTER THREE DAYS OF THERAPY	PER CENT OF PATIENTS WITH NORMAL WHITE BLOOD COUNTS AFTER ONE WEEK OF TREATMENT	PER CENT OF PATIENTS IN WHOM SEDIMENTATION RATE BECAME NORMAL IN SECOND WEEK OF DISEASE
800,000 p. o.*	100.0	80.0	60.0	100.0
500,000 p. o.	85.0	70.0	80.0	60.0
300,000 p. o.	77.8	86.9	78.4	89.0
Flavored	82.1	72.0	69.2	90.1
150,000 p. o.				
Plain	85.5	76.7	82.6	90.2
150,000 p. o.				
100,000 i. m.†	70.8	68.9	56.2	79.5
100,000 p. o.	82.5	79.8	65.2	92.1
50,000 p. o.	83.2	84.0	56.6	69.9

*Orally.
†Intramuscularly.

Rate of Disappearance of Beta-Hemolytic Streptococci From the Upper Respiratory Tract.—The data presented in Table II indicate that orally administered penicillin produced very rapid eradication of the beta-hemolytic streptococcus from the respiratory tract of patients with scarlet fever. Very little difference in the speed of disappearance of organisms could be detected when different dosages of the drug were used. It is striking that the parenteral administration of antibiotic was no more effective in this respect than the oral route. When recurrences of *Streptococcus pyogenes* were studied, however, it was found that the greatest number occurred with the use of 100,000 units of penicillin intramuscularly or 50,000 units orally given three times a day; the

latter dosage schedule was almost completely without effect in preventing bacteriologic relapses. The apparent rapid elimination of organisms from the respiratory tract in the early phase of treatment with 50,000 units of penicillin given by mouth and the rapidity of the return of streptococci almost immediately on cessation of treatment can be explained best on the following basis: During the period of therapy with this quantity of antibiotic, enough antibacterial effect was produced to reduce so markedly the number of *Str. pyogenes* in the nose and/or throat that they could not be grown by the cultural techniques employed; when treatment was stopped, however, the organisms multiplied profusely and again were easily detectable on culture.

TABLE II. EFFECT OF VARIOUS PENICILLIN DOSAGE SCHEDULES ON RATE OF DISAPPEARANCE OF BETA-HEMOLYTIC STREPTOCOCCI FROM UPPER RESPIRATORY TRACT

DOSE OF PENICILLIN EVERY 8 HOURS, AND ROUTE OF ADMINISTRATION	NO. OF PATIENTS WITH POSITIVE CULTURES ON ADMISSION	NO. OF PATIENTS AND HOURS AFTER INSTITUTION OF THERAPY IN WHICH CULTURES BECAME NEGATIVE			RECURRENCES OF BETA-HEMOLYTIC STREPTOCOCCI IN NOSE AND/OR THROAT FOLLOWING CESSATION OF TREATMENT
		24 HR.	48 HR.	72 HR.	
800,000 p.o.*	5	5	--	--	0
500,000 p.o.	18	16	2	--	1
300,000 p.o.	30	29	1	--	1
150,000 p.o.	66	64	2	--	1
100,000 p.o.	40	38	2	--	0
100,000 i.m.†	71	63	5	3	12
50,000 p.o.	16	14	2	--	12

*Orally.
†Intramuscularly.

Effect of Oral Penicillin Treatment on the Duration of the Rash in Scarlet Fever.—The duration of the scarlatinal rash was not shortened by the oral administration of penicillin in the cases reported here. This antibiotic agent has been shown to be without effect on the erythrogenic toxin of *Str. pyogenes* and these clinical observations confirm this finding.

Complications Occurring During the Course of Oral Penicillin Therapy.—Catarrhal otitis media occurred in six patients in this study; no relation to penicillin dosage schedule could be established. No instance of suppurative middle ear disease starting during or after treatment was noted. Recurrent streptococcal pharyngitis appearing after cessation of therapy was present in three instances: one patient had received 300,000, another 150,000, and the third 50,000 units of penicillin orally every eight hours for ten days. Only one case of recurrent scarlet fever was seen in the entire group; this developed eleven days after drug administration was stopped in a child who had been given thirty doses of 300,000 units of penicillin by mouth every eight hours. Pyelonephritis due to *Escherichia coli* appeared in a young girl treated with 150,000 units of flavored penicillin; the renal infection was brought under complete control rapidly with streptomycin.

Three cases of probable rheumatic fever were seen in this group of patients. In one, treated with 100,000 units of penicillin intramuscularly every eight hours,

there was prolongation of the Q-T interval and fever from the seventh to twelfth day after onset of pharyngitis; this was followed by complete recovery with no evidence of cardiac enlargement, murmurs, or arthralgia. In another child who had received 300,000 units of penicillin orally three times a day, increase in size of the heart and fullness in the region of the left auricle detected on roentgen ray study and a soft apical systolic murmur were present from eight to twenty-one days after the beginning of the streptococcal infection; the electrocardiogram was normal throughout and all manifestations disappeared in about two weeks. The third youngster had been given 100,000 units of penicillin orally every eight hours and on the seventeenth day following the first complaint of sore throat (treatment started within twenty-four hours after inception of pharyngitis) had abdominal pain, fever, migrating polyarthralgia, and straightening of the left cardiac border on roentgenologic examination; all of the signs and symptoms were gone in about one week after they were first noted. In addition to these three patients there were three others in whom the diagnosis of rheumatic fever was strongly suspected but could not be proved; one had arthralgias from the sixth to the eleventh day after the appearance of pharyngitis and persistence of an appreciably elevated sedimentation rate for the next seven months. Another, who had been treated with 300,000 units of penicillin orally every eight hours for ten days, developed fever, leucocytosis, abdominal pain, and pain in both knees which lasted from the twentieth to the twenty-fifth day after the onset of streptococcal infection. The third patient, treated orally with only 50,000 units of penicillin three times a day, had fever and a migrating polyarthralgia from the sixteenth to the nineteenth day of his disease. In none of these cases were abnormalities in the electrocardiogram detected, but tracings were not made until after the possibility of rheumatic fever was suspected.

Fever, the cause of which could not be detected, occurred from the third to the eleventh day after cessation of penicillin therapy in nineteen patients; there was no preponderance in any one of the different treatment schedules.

Although a number of the patients showed occasional red blood cells in the urine during the third week of their disease no clear-cut instance of glomerular nephritis was detected.

Blood Levels of Penicillin.—Several hundred strains of Group A *Str. pyogenes* isolated from patients with scarlet fever and examined for drug sensitivity during the past four years have all been inhibited by a concentration of penicillin ranging from 0.0075 to 0.03 units per cubic centimeter. This quantity of antibiotic agent has been assumed, therefore, to represent the blood level adequate to control infection with the beta-hemolytic streptococcus. Examination of Table III reveals that an adequate serum penicillin concentration was obtained in all of the patients for at least the first two hours after administration of the drug, with all of the dosage schedules employed except for 150,000 units of the flavored and 100,000 and 50,000 units of the plain preparation given orally. The persistence of a blood level beyond two hours was found to be related to the amount of penicillin administered, although a small number of individuals receiving smaller doses by mouth, 100,000 and

TABLE III. EFFECT OF VARIOUS DOSAGE SCHEDULES ON PENICILLIN BLOOD LEVELS ON SECOND DAY OF THERAPY

BLOOD LEVELS OF PENICILLIN UNITS/C.C.	QUANTITY AND ROUTE OF PENICILLIN ADMINISTERED—NO. OF PATIENTS SHOWING LEVELS AT DIFFERENT TIMES																			
	100,000 I.M.*			800,000 P.O.†			500,000 P.O.			300,000 P.O.			150,000 P.O.		FLAVORED 150,000 P.O.		100,000 P.O.		50,000 P.O.	
	70 PATIENTS			5 PATIENTS			20 PATIENTS			46 PATIENTS			37 PATIENTS		58 PATIENTS		49 PATIENTS		30 PATIENTS	
	2 HR.	4 HR.	6 HR.	2 HR.	4 HR.	6 HR.	2 HR.	4 HR.	6 HR.	2 HR.	4 HR.	6 HR.	2 HR.	4 HR.	2 HR.	4 HR.	2 HR.	4 HR.	2 HR.	4 HR.
0.015-0.03	1	4	0	0	0	1	0	0	5	0	17	3	13	7	30	2	4	1	2	0
0.078-0.156	28	5	1	1	0	4	1	8	8	16	18	1	18	0	13	0	30	1	6	0
0.313-0.625	27	1	0	1	5	0	9	11	1	30	0	0	6	0	1	0	6	0	2	0
1.25 -2.5	11	0	0	3	0	0	10	1	0	0	0	0	0	0	0	0	0	0	0	0
No level detectable	3	60	69	0	0	0	0	0	6	0	11	42	0	30	14	56	9	47	20	30

*Orally.
†Intramuscularly.

150,000 units, had demonstrable antibiotic in the blood for at least four hours after taking it. Although there was little difference in the number of patients with adequate blood levels when the groups given 100,000 units of penicillin orally and parenterally were compared, total quantity of penicillin in the serum was definitely higher and persistence somewhat longer when the antibiotic agent was given intramuscularly. The frequency of adequate serum concentrations in the orally treated group is quite striking, however, in view of the observation that, to produce a given effect, the oral dose of penicillin must be four to five times greater than the parenteral one. The minimally effective quantity of penicillin, based on the maintenance of a blood level of penicillin adequate to inhibit the beta-hemolytic streptococcus for at least two hours, appeared to be about 150,000 units in this study. Amounts smaller than this yielded an increasing number of cases in which no drug could be detected in the serum two hours after administration. Although not shown in the table, penicillin blood levels determined on the ninth day of therapy were generally lower, of somewhat shorter duration, and more often absent at two hours than when the studies were carried out on the second day of treatment. Since penicillin is excreted by the renal tubular mechanism, this may indicate some impairment of the excretory function of the kidney early in scarlet fever. That the kidney may be injured in varying degree during the acute phase of this disease is borne out by the not infrequent demonstration of transient hematuria.

Development of Sensitivity to Orally Administered Penicillin.—In a previously studied group of patients to whom penicillin was administered parenterally, an incidence of 2.5 per cent of allergic skin reactions were noted.[31] In the patients with scarlet fever treated by the oral route not a single instance of sensitization to this antibiotic agent was observed.

DISCUSSION AND SUMMARY

Studies of the administration of penicillin in fairly large doses by the oral route every eight hours have shown that this method of treatment produces rapid return to normal of the clinical and laboratory abnormalities in scarlet fever. Comparison of the results produced by the use of 100,000 units of the drug given every eight hours parenterally with those obtained when the same quantity was exhibited orally did not reveal any advantage in intramuscular therapy. Although the effects noted with oral medication were striking and most adequate, they did not appear to be quite as rapid as those observed when penicillin was given in a dose of 15,000 units intramuscularly every three hours.[30, 31] The differences, however, are too small to be of any great consequence.

The incidence of suppurative complications in scarlet fever was reduced almost to zero by oral administration of penicillin every eight hours for ten days. The same was not true, however, of the nonsuppurative sequelae; three probable cases of rheumatic fever occurred in this study. In addition, three children were observed in whom manifestations suggestive but not diagnostic of this late streptococcal complication were present. Routine electrocardiograms were not taken on all of the patients with scarlet fever in this investigation; had this been done, it is very likely that a larger number of instances of rheumatic

carditis would have been discovered. The importance of daily electrocardiograms and the significance of electrocardiographic abnormalities in individuals with streptococcal pharyngitis who are treated with penicillin has been discussed in complete detail in another paper.[32] Quite striking in the present series was the complete absence of acute diffuse glomerular nephritis.

Examination of the blood levels of penicillin following its administration by mouth revealed adequate plasma concentrations for a minimum of two hours following ingestion of a single dose when quantities of 150,000 units or more were given. The excellent clinical results and the rapid elimination of beta-hemolytic streptococci, observed with all of the oral dosage schedules except 50,000 units every eight hours, were produced, apparently, by persistence of penicillin in the blood for only about six to eight hours per day in the majority of patients. These results indicate quite clearly that "discontinuous" oral penicillin therapy is effective in streptococcal pharyngitis.

CONCLUSIONS

1. The oral administration of crystalline penicillin G every eight hours for ten days produced rapid clinical improvement and eradication of *Str. pyogenes* from the respiratory tracts of patients with scarlet fever.

2. The optimal oral dose of penicillin for the treatment of scarlet fever appeared to be 150,000 units of a buffered preparation given every eight hours for ten days.

3. The administration of penicillin by mouth reduced the incidence of suppurative complications in scarlet fever to almost zero.

4. The occurrence of rheumatic fever was not completely eliminated.

5. An adequate blood level of penicillin for only six to eight hours per day appeared to be completely effective in shortening the clinical course, eradicating beta-hemolytic streptococci and eliminating almost completely the suppurative complications of scarlet fever.

REFERENCES

1. Barach, A. L., Garthwaite, B., Oppenheimer, E. T., Forman, J., and Osburg, H.: Oral Administration of Penicillin, Science **102**: 247, 1945.
2. Bunn, P. A., McDermott, W., Hadley, S. J., and Carter, A. C.: The Treatment of Pneumococcic Pneumonia With Orally Administered Penicillin, J. A. M. A. **129**: 320, 1945.
3. Burke, F. G., Ross, S., and Strauss, C.: Oral Administration of Penicillin, J. A. M. A. **128**: 83, 1945.
4. Cohlan, S. Q., Lewis, J. M., and Seligman, E.: Blood Levels of Penicillin With Oral Use of Buffered and Unbuffered Solutions, Am. J. Dis. Child. **75**: 15, 1948.
5. Finland, M., Meads, M., and Ory, E. M.: Oral Penicillin, J. A. M. A. **129**: 315, 1945.
6. Friedman, M., and Terry, L. L.: Oral Aluminum Penicillin, South. M. J. **42**: 507, 1949.
7. Gyorgy, P., Vandergrift, H. N., Elias, W., Colio, L. G., Barry, F. M., and Pilcher, J. D.: Administration of Penicillin by Mouth, J. A. M. A. **127**: 639, 1945.
8. Heatley, N. G.: Administration of Penicillin by Mouth, Lancet **1**: 590, 1945.
9. Henderson, J. L., and McAdam, I. W. J.: Oral Administration of Penicillin, Lancet **1**: 922, 1946.
10. Hildick-Smith, G., Scott, T. F. Mc., and Whitlock, C. M.: Penicillin Regimens in Pediatric Practice: Study of Blood Levels, Pediatrics **5**: 97, 1950.
11. Hoffman, W. S., and Volini, I. F.: Studies in the Oral Administration of Penicillin. I. Assays of Various Preparations and the Determination of the Effective Therapeutic Dose, Am. J. M. Sc. **213**: 513, 1947.

12. Hoffman, W. S., and Volini, I. F.: Studies in the Oral Administration of Penicillin. II. Results of Treatment of Pneumococcic Lobar Pneumonia and Other Acute Infections With Several Oral Penicillin Preparations, Am. J. M. Sc. **213**: 520, 1947.
13. Hoffman, W. S., Hofer, J. W., and Gordon, H.: The Treatment of Acute Respiratory Infections in Children With Orally Administered Penicillin, J. PEDIAT. **32**: 1, 1948.
14. Husson, G. S.: Oral Penicillin in Infants, J. PEDIAT. **31**: 651, 1947.
15. Keefer, C. S.: Dosage Forms of Penicillin for Systemic Infections, Am. J. Med. **7**: 216, 1949.
16. MacLachlan, W. W. G., Bracken, M. M., Lynch, M. P., and Bailey, W. R.: A Comparison of Intramuscular and Oral Penicillin in Pneumococcic Pneumonia, Canad. M. A. J. **61**: 134, 1949.
17. Markowitz, M., and Kuttner, A. G.: A Study of the Absorption and Excretion of Oral Penicillin in Children, J. PEDIAT. **31**: 195, 1947.
18. McDermott, W., Bunn, P. A., Benoit, M., DuBois, R., and Haynes, W.: Oral Penicillin, Science **101**: 228, 1945.
19. McDermott, W., Bunn, P. A., Benoit, M., DuBois, R., and Reynolds, M. E.: The Absorption of Orally Administered Penicillin, Science **103**: 359, 1946.
20. McDermott, W., Bunn, P. A., Benoit, M., DuBois, R., and Reynolds, M. E.: The Absorption, Excretion and Destruction of Orally Administered Penicillin, J. Clin. Investigation **25**: 190, 1946.
21. Meads, M., Ory, E., and Finland, M.: Oral Penicillin X, Science **103**: 501, 1946.
22. Rammelkamp, C. H.: A Method for Determining the Concentration of Penicillin in Body Fluids and Exudates, Proc. Soc. Exper. Biol. & Med. **51**: 95, 1942.
23. Reisman, H. A., Goldfarb, A. A., and Mollov, M.: Oral Administration of Penicillin in Pediatrics, Am. J. Dis. Child. **74**: 19, 1947.
24. Robinson, J. A., Hirsch, H. L., and Dowling, H. F.: Oral Penicillin in the Treatment of Various Bacterial Infections, Am. J. Med. **4**: 716, 1948.
25. Ross, S., Burke, F. G., McLendon, P. A.: Penicillin by Mouth. Report of a Clinical Trial, J. Am. M. A. **129**: 327, 1945.
26. Seager, L. D., Shoemaker, W. G., and Wells, G.: Blood Levels of Penicillin After Various Forms of Oral Administration, Am. J. M. Sc. **212**: 90, 1946.
27. Suchett-Kaye, A. I., and Latter, R. B.: Oral Penicillin in Young Children, Brit. M. J. **2**: 953, 1947.
28. Terry, L. L., and Friedman, M.: Oral Penicillin in the Treatment of Acute Respiratory Infections, Mil. Surgeon **103**: 377, 1948.
29. White, H. J., Lee, M. E., and Alverson, C.: Therapeutic Effect of Single Oral Doses of Penicillin, Proc. Soc. Exper. Biol. & Med. **62**: 35, 1946.
30. Weinstein, L., and Potsubay, S. F.: A Comparison of Symptomatic Treatment, Gamma Globulin, and Penicillin in the Treatment of Scarlet Fever, J. PEDIAT. **37**: 291, 1950.
31. Weinstein, L., and Bachrach, L.: The Treatment of Scarlet Fever With Frequent Doses of Penicillin G Given Intramuscularly or Orally. To be published.
32. Weinstein, L., Bachrach, L., and Boyer, N. H.: Observations on the Development of Rheumatic Fever and Glomerular Nephritis in Cases of Scarlet Fever Treated With Penicillin, New England J. Med. **242**: 1002, 1950.

SODIUM SULFACETIMIDE FOR THE PROPHYLAXIS OF GONORRHEAL OPHTHALMIA NEONATORUM

Preliminary Report

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IN 1881, Credé[1] discovered that gonorrheal ophthalmia neonatorum could be prevented with the prophylactic instillation of a 2 per cent silver nitrate solution into the conjunctival sacs of newborn infants. With the introduction of this prophylactic measure there has been a remarkable reduction in the incidence of gonorrheal ophthalmia neonatorum and its complications. However, there are several disadvantages to the classical Credé method: (1) incomplete protection from gonorrheal ophthalmia neonatorum, (2) chemical conjunctivitis is a frequent complication, and (3) occasional cases of blindness have occurred when a stronger solution of silver nitrate was used by mistake (this, however, has been almost completely eliminated by the use of a 1 per cent solution in wax ampules).

On account of the above disadvantages numerous investigators have proposed substitutes for silver nitrate. In 1940, Hartman[2] found that silver acetate was on a par with silver nitrate as a prophylactic agent. It was less irritating and, since a concentrated solution cannot be made with silver acetate, it was safer than silver nitrate. Gleich, Blumberg, and Mason,[3] as a result of their study in 1943, suggested that sulfathiazole (total dose of 20 gr. given over three days, starting twelve hours after birth) be administered routinely by mouth as an adjunct to silver nitrate prophylaxis. By this method they were able to lower the incidence of neonatal gonorrheal ophthalmia considerably. With the advent of penicillin many investigators have attempted to establish its value in this problem. In a preliminary report in 1947, Franklin[4] stated that penicillin compared favorably with silver nitrate as a prophylactic agent and that penicillin is to be preferred because danger of permanent eye injury is eliminated, instillation is nonpainful, and other ocular complications are less frequent during the first days of life. He corroborated this study later by bacteriologic analyses.[5] Sacks-Wilner and Sacks-Wilner[6] proposed the use of penicillin because it is a therapeutic agent as well as a prophylactic agent.

More recently, Allen and Barrere[7] found that penicillin had no advantage over silver nitrate in the prophylaxis of gonorrheal ophthalmia neonatorum, but they felt that an adequate comparison was not possible because of the low incidence of gonorrheal infection in their material. As a result of their recent investigation, Watts and Gleich[8] suggest the instillation of silver nitrate (1 drop of a 1 per cent solution) into the conjunctival sacs of all newborn infants before leaving the delivery room, followed by an intramuscular injection of penicillin (50,000 units of aqueous penicillin G) on reaching the nursery. By using this

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method they were able to prevent gonorrheal ophthalmia neonatorum completely in a group of 4,565 infants. Still more recently, Sweet and his group[9] reported that intramuscular penicillin alone (50,000 units of crystalline penicillin) seemed to be as effective as silver nitrate in reducing the incidence of gonorrheal ophthalmia neonatorum.

The following study with sodium sulfacetimide* for the prophylaxis of gonorrheal ophthalmia neonatorum was made in an attempt to find still another satisfactory substitute for silver nitrate.

METHOD

On March 1, 1949, this study was begun on all newborn infants (full term and premature) at the Louisville General Hospital. The infants were divided into three groups as follows: group 1, all white infants; group 2, male Negro infants; and group 3, female Negro infants. The one-year period of the study was then divided into three periods of four months each. The three prophylactic agents, 1 per cent silver nitrate solution, 30 per cent sodium sulfacetimide solution, and 10 per cent sodium sulfacetimide ointment were used in rotation so that each group received each prophylactic agent for a period of four months.

Each infant received its respective prophylaxis of the eyes before leaving the delivery room. When silver nitrate was used, one drop of a 1 per cent solution from a wax ampule was instilled into each conjunctival sac and three minutes later the eyes were irrigated with isotonic saline. The 30 per cent sodium sulfacetimide was used in a like manner but the eyes were not irrigated following its instillation. In the case of 10 per cent sodium sulfacetimide ointment, a one-half inch "ribbon" was applied to each eye. The ointment was not wiped away, neither were the eyes irrigated.

All reactions to the prophylactic preparations were noted, and any discharge present was examined on smear and cultured for *Neisseria gonorrhoeae*. Organisms other than *N. gonorrhoeae* were not reported.

RESULTS

This study comprised a total of 1,907 infants born during a one-year period from March 1, 1949, to March 1, 1950. Their average hospital stay was 4.9 days. All infants that died before the fifth day of life were excluded from this study. Only two cases of gonorrheal ophthalmia neonatorum occurred in the whole group (Table I).

Six hundred eighty-two infants received 1 per cent silver nitrate, and of these 37 or 5.4 per cent developed reactions. The average time of onset of the reactions in this group was 2.1 days. These reactions were characterized by a mild to profuse purulent discharge from one or both eyes with red, edematous lids in many cases. A few even developed vesicles on the lids, and silver nitrate burns of the face were occasionally seen. These reactions usually persisted for two to four days and then cleared up with no sequelae. One infant in this group developed gonorrheal ophthalmia neonatorum on the first day of life.

*The sodium sulfacetimide preparations (30 per cent solution and 10 per cent ointment) were furnished by the Schering Corporation.

TABLE I. THE USE OF SILVER NITRATE AND SODIUM SULFACETIMIDE (30 PER CENT DROPS AND 10 PER CENT OINTMENT) IN THE PROPHYLAXIS OF GONORRHEAL OPHTHALMIA NEONATORUM

	1 PER CENT SILVER NITRATE DROPS	30 PER CENT SODIUM SULFACETIMIDE DROPS	10 PER CENT SODIUM SULFACETIMIDE OINTMENT	TOTAL GROUP
No. of infants	682	642	583	1,907
No. of reactions	37	22	26	85
Per cent reactions	5.4	3.4	4.5	4.5
Average time of onset of reaction in days	2.1	3.9	3.3	3.0
No. with gonorrheal ophthalmia neonatorum	1	0	1	2

The group of 642 infants that received 30 per cent sodium sulfacetimide solution as prophylaxis developed twenty-two reactions or 3.4 per cent with an average time of onset of the reactions of 3.9 days. There were no cases of gonorrheal ophthalmia neonatorum in this group.

Of the 583 infants receiving 10 per cent sodium sulfacetimide ointment, 26 or 4.5 per cent developed reactions with an average time of onset of 3.3 days. The other case of gonorrheal ophthalmia neonatorum occurred in an infant in this group on the third day of life.

The reactions to both sodium sulfacetimide solution and ointment were not as severe and occurred later than those from silver nitrate. These reactions were manifested by a mild to moderate purulent discharge from one or both eyes with or without redness and edema of the lids, all of which cleared up in two to four days with no sequelae. No severe allergic reactions were noted.

COMMENTS

In an attempt to find a satisfactory substitute for silver nitrate in the prophylaxis of gonorrheal ophthalmia neonatorum, sodium sulfacetimide (30 per cent solution and 10 per cent ointment) was chosen for the following reasons: it is easily applied (the 30 per cent solution was easier applied than the 10 per cent ointment); it is stable at room temperature; it has a known antibacterial effect on the gonococcus;[10] it is nonirritating,[11, 12] and allergic reactions are rarely encountered.

Schilling[13] used sulfacetimide in the prophylaxis of 1,300 infants and found only two cases of gonorrheal ophthalmia neonatorum. When compared with the results of other investigators using silver nitrate, sulfacetimide was much more effective in prophylaxis.

Since only two cases of gonorrheal ophthalmia neonatorum occurred during the present study, one, in an infant receiving silver nitrate, and the other in an infant receiving 10 per cent sodium sulfacetimide ointment, neither of the three preparations used can be evaluated properly as to their effectiveness in the prevention of gonorrheal ophthalmia neonatorum. However, the incidence of chemical conjunctivitis was significantly greater with silver nitrate than with either of the sodium sulfacetimide preparations, especially the 30 per cent sodium sulfacetimide solution.

SUMMARY

The incidence of gonorrheal ophthalmia neonatorum has been greatly reduced since the introduction of silver nitrate prophylaxis by Credé in 1881. However, since there are several disadvantages to this method, various substitutes have been proposed including 1 per cent silver acetate drops, sulfathiazole parenterally, penicillin as drops, penicillin intramuscularly, penicillin in combination with 1 per cent silver nitrate drops, and sulfacetimide. All of these substitutes have been reported to be superior to 1 per cent silver nitrate.

The 1,907 infants in this study were divided into three groups with each group receiving one of the three prophylactic agents, 1 per cent silver nitrate drops, 30 per cent sodium sulfacetimide drops, or 10 per cent sodium sulfacetimide ointment. All reactions to these prophylactic agents were noted and any discharge present was examined for *N. gonorrhoeae* by smear and culture. Only two infants developed gonorrheal ophthalmia neonatorum. One of these had received silver nitrate prophylaxis, and the other, 10 per cent sodium sulfacetimide ointment. Silver nitrate, however, produced more reactions in the form of chemical conjunctivitis and these reactions were more severe than those produced by the sulfacetimide preparations. No severe allergic reactions to sulfacetimide occurred.

From this study sodium sulfacetimide, especially the 30 per cent solution, was found to produce less chemical conjunctivitis than 1 per cent silver nitrate, and also seemed to be just as effective in preventing gonorrheal ophthalmia neonatorum, but further study is needed to confirm this latter point.

REFERENCES

1. Credé, K. S. F.: Die Verhutung der Augenentzundung der Neugeborenen, Arch. f. Gynäk. **17**: 50, 1881; ibid, **18**: 367, 1881.
2. Hartman, W. F.: The Prophylaxis of Ophthalmia Neonatorum With Silver Acetate, Pennsylvania M. J. **43**: 639, 1940.
3. Gleich, M., Blumberg, M., and Mason, A.: Prophylactic Value of Sulfathiazole Against Neonatal Gonococcic Conjunctivitis, Am. J. Dis. Child. **31**: 162, 1944.
4. Franklin, H. C.: Prophylaxis Against Ocular Neonatorum, J. A. M. A. **134**: 23, 1947.
5. Franklin, H. C., and Loeb, L. N.: Bacterial Flora in Eyes of Newborn Infants During First Forty Hours of Life After Single Instillation of Penicillin and Silver Nitrate, J. PEDIAT. **32**: 251, 1948.
6. Sacks-Wilner, A., and Sacks-Wilner, E. P.: Penicillin as a Prophylactic Against Ophthalmia Neonatorum, Arch. Ophth. **41**: 444, 1949.
7. Allen, J. H., and Barrere, L. E.: Prophylaxis of Gonorrheal Ophthalmia of the Newborn, J.A.M.A. **141**: 522, 1949.
8. Watts, S. G., and Gleich, M. M.: Penicillin—Silver Nitrate Prophylaxis Against Gonorrheal Ophthalmia of the Newborn, J.A.M.A. **143**: 635, 1950.
9. Sweet, L. K., Barter, R. H., Cummings, P., Featherston, W. M., Parker, G. F., Oven, R. A., Fairchild, J. P., Mohr, J. F., McDonald, J. J., and Miller, R. T.: The Use of Systemically Administered Penicillin as a Prophylactic Against Ophthalmia Neonatorum, from an abstract of paper read before the American Pediatric Society, May 10, 1950, at French Lick, Ind.
10. Scott, G. I., and Sorsby, A.: Discussion on Value of Sulphonamides in Ophthalmology, Tr. Ophth. Soc. U. Kingdom (1942) **62**: 3, 1943.
11. Kuhn, H. S.: Sodium Sulfacetimide 30 Per Cent Solution in Ophthalmology, Tr. Am. Acad. Ophth. **50**: 210, 1946.
12. Dickson, R. M.: Traumatic Ulcer of Cornea With Special Reference to Coal Miners, Brit. J. Ophth. **26**: 529, 1942.
13. Schilling, B.: A Comparative Evaluation of the Credé and Olah (Sulfacetimide) Methods of Prophylaxis (of Newborn Eyes). Special Reprint from the Scientific Publication of the Szent Rokus Public Hospital, Hungary.

ORAL PENICILLIN IN THE PROPHYLAXIS OF RECURRENT RHEUMATIC FEVER

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WHEN one studies the high mortality rates of rheumatic fever, the figures are startling. Mustard[1] informs us that for each death of a person under 20 years of age due to the combined causes of pertussis, diphtheria, and poliomyelitis, there are fifty deaths due to rheumatic fever of the heart. Wilson and Lubschez[2] state that the United States vital statistics reports for 1944 list deaths from rheumatic fever of the heart as 20.4 per 100,000, deaths from rheumatic fever without heart complications as 0.1 per 100,000 population, both stated in comparison with the crude death rate of 1,040 per 100,000 from all causes. The Metropolitan Life Insurance Company[3] reported deaths in school children due to rheumatic fever including rheumatic disease of the heart as 5 to 6 per 100,000 among industrial policy holders. Wilson and Lubschez,[2] in their study of 1,042 cases of rheumatic fever which were under study over a thirty-year period of observation, reported 89 per cent were seen either at death or at the end of a period of thirty years of study. The mean age of onset was 6.5 years. Among 226 deaths, 75.7 per cent were due to rheumatic heart disease and 10.2 per cent to subacute bacterial endocarditis. The incidence of the latter was 2.2 per cent of the series. Cardiac involvement was demonstrable in every patient of the series and multiple valvular lesions in one-half. The highest death rates occurred one year after the onset and between the ages of 1 and 4 years (33.2 per thousand), and between the ages of 10 to 14 years (16.3 per thousand). An affected child has four chances out of five to survive fifteen years after the onset, three chances out of four to survive twenty years and two chances out of three to survive thirty years after the onset. The over-all chance to survive to the age of 40 years is one out of two. An affected child has four out of five chances to survive up to the age of 10 years, three out of four to survive to puberty, and nineteen out of twenty chances to survive early adult life.

With this specter of invalidism and an early demise facing rheumatic fever patients, an all-out effort is being made to avert the almost inevitable recurring attack which usually adds insult to injury and precipitates the eventual crisis of a cardiac death. The greatest obstacle is the matter of determining the etiological agent or agents. Many theories have been promulgated since Baillou[4] first described and named rheumatism in 1635. After carefully investigating the voluminous literature on the subject of the etiology of rheumatic fever, one is impressed by the lack of distinct, conclusive knowledge of the agents involved, and it is my opinion that none of the theories hold too much water.

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In earlier articles, I discussed the theory behind the use of penicillin troches and sulfonamides for the prevention of rheumatic fever. Most of these studies are predicated upon the idea that the rheumatic disease occurs shortly after an upper respiratory infection of one to three days' duration caused by particular strains of hemolytic streptococci, followed by a latent interval of one to three weeks during which some phenomenon, either allergic, immunologic, or otherwise takes place, subsequently followed by the clinical, manifestations of the rheumatic infection in any of its protean forms. To date, the sulfonamides, in small dosage, has been the drug of choice, but this has not been without danger. Many institutions have now discarded this method of prophylaxis.

In the previous study,[5] it was found that penicillin troches of 5,000 units each, when held in the mouth of the potentially rheumatic patient were efficacious in sterilizing the mouth and throat for up to two hours at a time. By this simple procedure, without causing any demonstrable level of penicillin in the blood, and without sensitizing the patient to the drug, it was possible to apparently protect the individual against streptococcic infections of the throat.

Repeating the procedures of two previous years, in this the third year of the experiment (1948 to 1949), eighty-six children were observed. Forty-six received the troches regularly three times daily from September through June, and forty controls received placebo troches of similar size, shape, and taste. The group consisted of sixty-three children with a definite history of rheumatic fever and with various types of cardiac defects and twenty-three with congenital heart defects. Of the former, thirty were controls, and of the latter, ten were controls. The congenital group was included in the study in order to ascertain whether there was any value in the prevention of subacute bacterial endocarditis.

PROCEDURE

The children under study were examined in the clinic at least once a month. At this time each child was weighed, measured, and notation was made of the temperature, pulse, respiration, and blood pressure. A routine throat culture, erythrosedimentation time (Cutler method), and vital capacity were included at each visit. When rheumatic activity was suspected because of an elevated temperature, increased sedimentation rate, or the presence of streptococci in the throat culture, the patient returned to the clinic a week later for a complete re-examination.

BACTERIOLOGY

Of the eighty-six cases studied, throat cultures were taken at each clinical session, as described in a previous article. Some patients visited the clinic only once, others up to eighteen times during the season. The organisms recovered included the following: *Staphylococcus albus, Staphylococcus aureus, Streptococcus hemolyticus, Streptococcus viridans,* pneumococcus, nonhemolytic streptococcus, microcatarrhalis, *Bacillus aerogenes, Bacillus subtilis,* and hemolytic *Staphylococcus albus. Streptococcus hemolyticus,* generally accepted as the precipitating agent in rheumatic fever, was found in five congenital cases out of

twenty-three (21.6 per cent) and in seven of the rheumatic cases out of sixty-three (11.1 per cent). In further evaluating the cases in the congenital group, there was one positive growth of *S. hemolyticus* out of four cultures taken; in another patient, a control case, two out of three revealed *S. hemolyticus,* and in three other congenital cases only one positive culture in five trials. *S. viridans* was discovered in fourteen of the congenital cases and these disappeared in a culture taken two hours after sucking a penicillin troche. In the rheumatic group, one child showed hemolytic streptococcus four times out of nine visits; in five children, this organism was found only once out of nine cultures. In fifty-six rheumatic children, this organism was never found. In one child who had an active rheumatic fever with a sedimentation rate ranging from 20 to 85 mm. in one hour and who was receiving the penicillin troches, there was no apparent effect on the activity. This boy visited the clinic eighteen times and had a throat culture each time; there were but two cultures positive for hemolytic streptococci in all the visits. In spite of the fact that most observers believe this organism is the etiological agent in rheumatic fever, the apparent absence of the bacteria in the throats of so many rheumatic children seems to question its significance. Perhaps the most interesting fact is that of all the organisms isolated the *Staph. aureus* occurred in 95 per cent of all the cultures taken. Not alone was this the most constant organism but also the most stubborn since these persisted at succeeding visits. In twenty children, cultures were taken before and after the use of the troches in order to note the immediate effect, and in practically all these cases the *S. hemolyticus* and *S. viridans,* if present in the first culture, disappeared in the second, proving the efficacy of the troches upon these bacteria localized in the throat. The *Staph. aureus,* however, never responded to the penicillin. This is interesting in view of the fact that this was one of the first bacteria to be associated with rheumatic fever.[6]

CONCLUSION

The important consideration is the question of the efficacy of penicillin troches in preventing recurrent attacks of rheumatic fever. In our control group of thirty rheumatic children, two had a recurrence of rheumatic fever, one with polyarthritis, and the other, carditis (6.6 per cent) and in neither of these cases was a culture of *S. hemolyticus* present. In the thirty-three rheumatic children receiving penicillin troches not one presented any evidence of rheumatic activity. One child, a 14-year-old boy with an active carditis (aortic insufficiency), was given the troches with no apparent effect either way upon the progress of the condition.

This study confirms a previous opinion that 5,000 unit penicillin throat troches* are of value in temporarily eliminating *S. hemolyticus* from throats of rheumatic children, and it is my belief that in all rheumatic fever programs in which sulfonamides are an important integral part, replacement by these

*The troches used in the previous series as well as in this present series are marketed under the name of Ledercillin Crystalline Penicillin G Troches, 5,000 units each. They were supplied by the Lederle Laboratories Division of the American Cyanamide Company, 30 Rockefeller Plaza, New York, N. Y., who also aided by a grant.

troches is desirable. They are equally as efficient, and because of the dangers entailed in the use of sulfonamides, small doses of penicillin may serve as a safe and convenient method of preventing recurrent attacks of rheumatic fever.

REFERENCES

1. Mustard, H. S.: Rheumatic Fever in the Perspective of Public Health, Am .J. Med. 2: 609, 1947.
2. Wilson, May G., and Lubschez, R.: Longevity in Rheumatic Fever, J. A. M. A. 138: 794, 1948.
3. Health Problems of School Age Children, Statis. Bull., Metropolitan Life Insurance Co., 28: 4, 1947.
4. Baillou: De Rheumatismo, 1635.
5. Maliner, M. M., and Amsterdam, S. D.: Oral Penicillin in the Prophylaxis of Recurrent Rheumatic Fever, J. PEDIAT. 31: 658, 1947. Maliner, M. M., Amsterdam, S. D., and Arriche, C. C.: Further Studies on Oral Penicillin in the Prophylaxis of Recurrent Rheumatic Fever, J. PEDIAT. 35: 145, 1949.
6. Garrod, A. E.: A Treatise on Rheumatism, London, 1890, Charles Griffin & Co., p. 36.

THE USE OF SEDATIVE-INDUCED SLEEP AS AN AID TO ELECTROENCEPHALOGRAPHIC DIAGNOSIS IN CHILDREN

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THE fact that convulsive seizures often occur during sleep even in patients who are not subject to such attacks while awake has been recognized since ancient times.[1] Recently Gibbs and Gibbs[2] have shown that subclinical seizure discharges occur in the electroencephalogram much more ferquently during sleep than when the patient is awake, and that epileptiform or focal abnormalities which are not apparent in a waking electrogram may become manifest when the patient is asleep. In a study of over 500 cases of verified epilepsy, these workers concluded that abnormal electrical discharges were more than twice as likely to appear during sleep as during the waking state.[3]

In the light of these observations it is clear that sleep should provide a very satisfactory method of activating latent electrical abnormalities in children if a means of inducing sleep quickly and effectively could be found which would not at the same time depress the abnormal electrical activity of the brain. The demonstration that at least some types of electrographic seizure pattern are not abolished by barbiturates in therapeutic doses,[4,5] and the common observation that a large proportion of patients receiving anticonvulsant medication continue to show larval electrographic discharges even when their clinical seizures are completely controlled,[6,7] suggested that small doses of certain sedative drugs might, in conducive environmental conditions, promote sleep without seriously obtunding its activating properties.

This report is concerned with the results of a study of sedation-induced sleep in 400 children between the ages of 3 and 15 years* with known or suspected cerebral convulsive disorders. Originally it was planned to screen all available sedatives in a search for one having low anticonvulsant properties but which would nevertheless promote sleep quickly and effectively without introducing, by its action on the brain, electrical activity foreign to the individual patient's characteristic sleep tracing.† However, early in this investigation Nembutal‡ was tried and such successful results were obtained with it that further search for the ideal sedative was temporarily abandoned. The possibility that a better agent for the purpose can be found is patent, for, although Nembutal has proved remarkably effective in promoting sleep and has failed to complicate the tracings with excessive barbiturate-induced fast activity in the doses used, it is known to have moderately high anticonvulsant properties and may for this reason suppress abnormalities which might otherwise appear.

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*A special report concerning the use of routine sedation in infants is now in preparation for publication.

†That is, not complicate the EEG tracing by introducing new activity such as the typical barbiturate-induced fast waves.

‡The Nembutal used in these studies was kindly supplied by the Research Division of Abbott Pharmaceutical Company.

METHOD

All recordings were made with the patient lying on a bed in a shielded, dimly-lit or darkened semisoundproof room. Every effort was made to insure the patient's comfort and relaxation. The electroencephalograph employed was a six-channel Offner Type D dynograph. This instrument is particularly suited to this type of study because the nonblocking nature of the amplifiers and the large excursion permitted by the dynograph make it possible to obtain clearly delineated tracings without recourse to excessive attenuation of the interparoxysmal activity in the presence of the extremely high voltage electrical discharges which are often recorded during sleep.

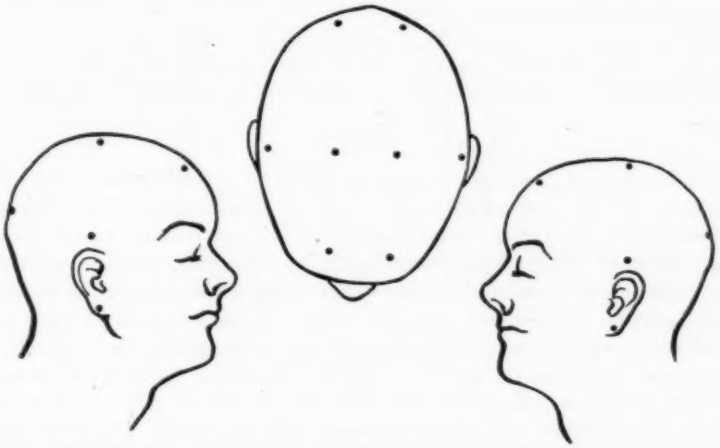


Fig. 1.—Standard electrode placements used for routine clinical electroencephalography in children.

Eight standard electrode placements were used routinely (Fig. 1). Further placements were employed to localize more sharply focal phenomena reflected in one or more of the standard leads. It has been our experience that the routine placement of a greater number of electrodes does not increase the likelihood of detecting discrete focal abnormalities. In this laboratory a very high percentage of focal phenomena have been detected using only the eight standard electrode placements and a routine series of coronal, transverse, and triangulation runs which serve to indicate the loci at which further electrodes should be placed in order to make a more discrete localization possible.*

The time of administration of the sedative varied somewhat at the discretion of the technician making the tracing. Usually a routine series of monopolar and bipolar runs quickly was made, after which the patient was given Nembutal calcium by mouth, the size of the dose depending upon the child's age: children from 3 to 11 years were given ¾ gr., those from 10 to 14 years 1 to 1½ gr. Sleep ensued in 90 per cent of the children tested (where previously, in the

*A report on the technic employed and the results obtained in focal lesions in children is now in course of preparation.

absence of sedation, the incidence of sleep in children had been approximately 5 per cent in spite of long recording periods). This high percentage of effectiveness in obtaining sleep with quite small doses of Nembutal is believed to be due in part to the quiet and pleasant conditions under which the tracings were made. Furthermore, appointments for children in whom sleep records were to be scheduled were made for the afternoon or evening where possible, because experience soon showed that children are more likely to go to sleep easily at these times than before lunch. A three-minute period of hyperventilation often proved conducive to sleep, especially in children who were restless or unduly nervous. Sometimes it was helpful with nervous children for someone to read to them while waiting for the full effect of the sedative to occur; often a more satisfactory waking record was obtained in this way.

After a variable period of sleep, usually thirty to forty minutes, the patient was gently awakened while the tracing was still being made, as the electrogram upon awakening may show abnormalities which are not present in the deep stages of sleep.

RESULTS

Effectiveness of Sedation-Sleep as an Activator.—Gibbs and Gibbs[3] have reported that normal sleep doubles the incidence of epileptiform activity in the electroencephalograms of convulsive patients. It is not possible in a mixed series of cases referred for diagnosis, such as the one reported here, to calculate accurately the effectiveness of sedation-induced sleep in promoting the appearance of electrographic abnormalities because many of the children in such an unselected group who did not show epileptiform or abnormal focal activity may not have been subject to a convulsive cerebral disorder in spite of the presence of epileptoid symptoms. However, the high percentage of patients who showed abnormal paroxysmal or focal patterns during sleep indicates that it may be an even more effective activating agent in children than in adults.[2] Obviously, the use of mild sedation did not in most cases prevent the appearance of abnormal activity.

Activation of Abnormal Activity Not in Evidence While Awake.—

Nonfocal paroxysmal discharge: One of the most significant findings of the Gibbs' group was that larval epileptiform activity and epileptogenic foci which are not manifest in a waking tracing may become clearly apparent and even a dominating feature of a sleep record. This has been repeatedly confirmed in the present study with the additional finding that sleep may activate latent abnormalities where other methods of activation such as intravenous Metrazol or overventilation fail to elicit them. Particularly significant is the observation that the bilaterally synchronous three per second spike and wave type of electrographic pattern may appear in sleep after rigorous hyperventilation has failed to produce any paroxysmal activity in the waking record.

As the clinical symptoms associated with this type of electrical seizure discharge are sometimes obscure and poorly defined, the differential diagnosis often rests entirely upon the electroencephalographic findings, and hence a falsely negative electrogram can weigh heavily against the patient, especially when subsequent progression to major convulsive attacks ensues.

The EEG sample in Fig. 2 is from a sleep tracing of a 12-year-old child who failed to show paroxysmal episodes while awake. This child was referred for electroencephalographic study by his family physician because of "absent-mindedness and failure to answer questions directed to him at the breakfast table." He had been severely reprimanded and even punished for this by his father, but his mother, feeling that his "dreaminess" in the morning was due to poor health, took him to see the family physician. Diagnosis in this case would have been equivocal had it been dependent solely upon the waking tracing in which the only marked abnormality was the excessively high voltage (185 microvolts maximum) of the basic eight to nine per second rhythm. Three

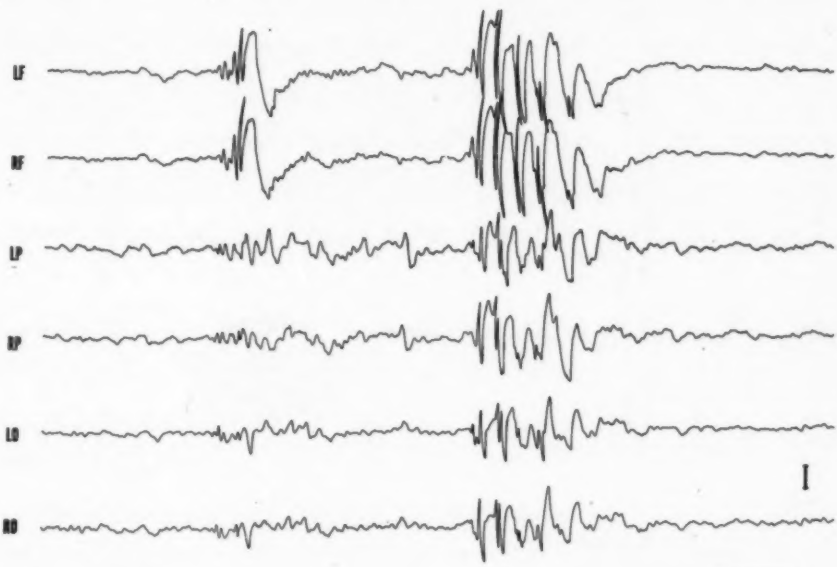


Fig. 2.—Male, aged 12 years. Referred because of "absent-mindedness" and "failure to answer questions directed to him on occasion."

minutes of satisfactory overbreathing (approximately 150 breaths) produced some slowing and increase in amplitude but the "build-up" and persistence of effect were not excessive for this age level. However, immediately upon the child's falling asleep extremely high voltage bursts of bilaterally synchronous three per second spike-wave complexes (Fig. 2) began to appear and were repeated at various intervals throughout the sleep period. In view of the history it is of interest that the spike-wave activity persisted for some time after the child had been awakened.

Focal discharge: It has been reported[7] that focal abnormalities produced by experimental brain trauma in animals are more difficult to detect under light Nembutal anesthesia. This is not the case when the drug is used in small

sedative doses to promote sleep. Indeed, it was found that the detection and subsequent localization of electrical foci were greatly facilitated in every case by the use of Nembutal-induced sleep.

The electrographic samples in Fig. 3 constitute a cogent demonstration of this fact. The waking record showed only a slight asymmetry and asynchrony of the temporal traces. During sleep, however, sharp wave discharges began to appear in the right temporal and to a lesser degree in the right parietal lead. Subsequent placement of more electrodes revealed a clear-cut focus in the region shown in the accompanying diagram of Fig. 3, a finding which is in accord with the type of seizure to which the patient was subject.

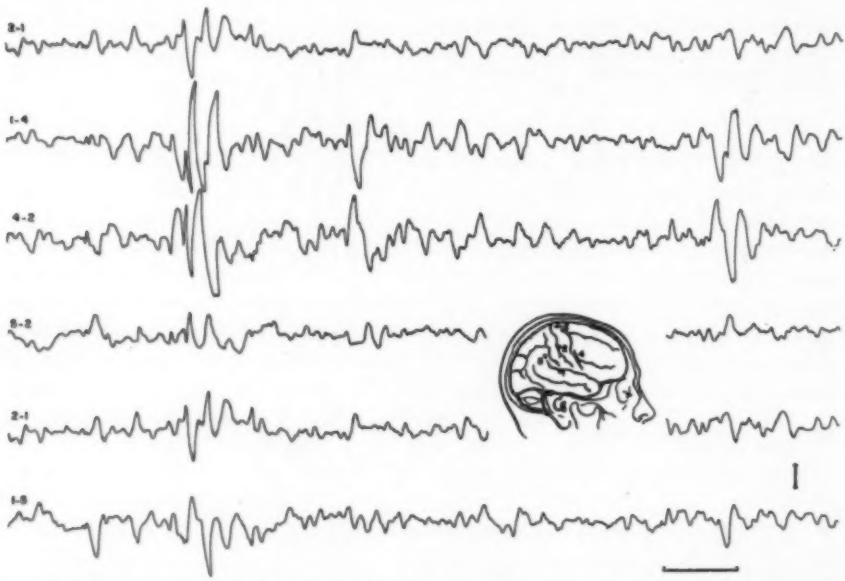
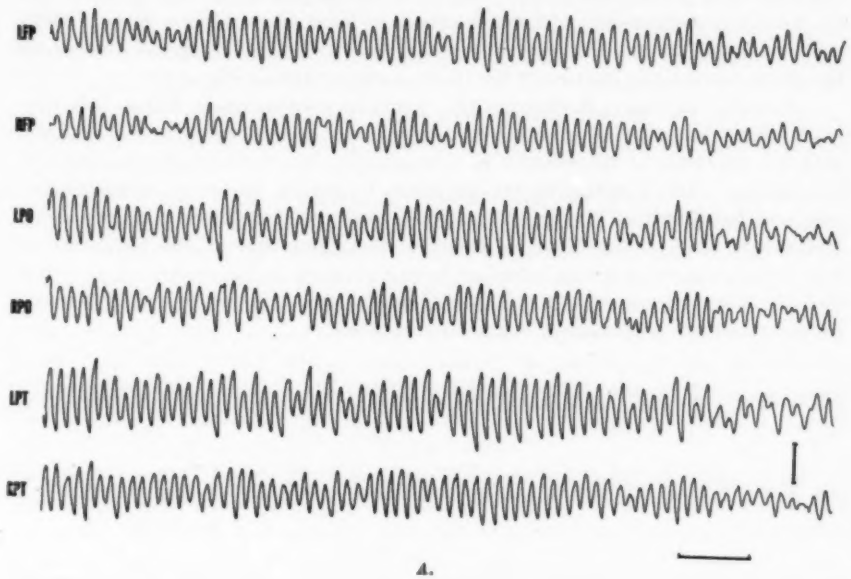


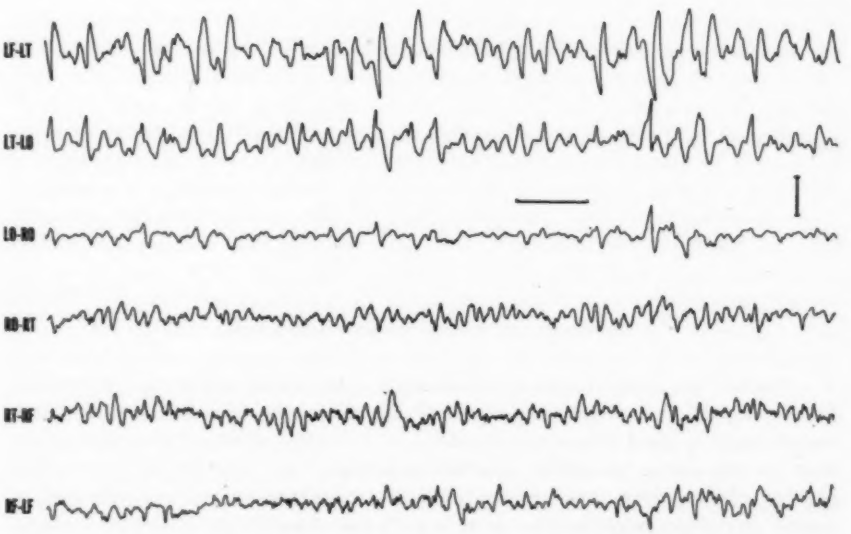
Fig. 3.—Male, aged 7 years. Twitching of left hand and arm accompanied by turning of the head to the left with disorientation but no true loss of consciousness. Atrophic gyri disclosed by craniotomy in approximate region of electrographic focus.

Perhaps even more important than that epileptogenic foci may be activated by sleep is the finding that during this state a primary focal lesion may be revealed in a case in which the waking record showed a diffuse abnormality of a type generally associated with cryptogenic or at least nonfocal epilepsy.

The samples in Figs. 4*A* and *B* were taken from a tracing of a child referred for electroencephalography because of "petit mal-like seizures." These were described by the mother as short episodes of "unresponsiveness and apparent bewilderment"—a story very similar to that of the first case described in this paper. A previous electrogram made some years before in another city was reported as "consistent with a diagnosis of idiopathic epilepsy." From the sample of the waking tracing shown in Fig. 4*A* it is easy to see why such a



A.



B.

Fig. 4.—*A*, Female, aged 11 years. Referred because of spells of "unresponsiveness and bewilderment" which appeared to be true psychomotor attacks. Note continuous very high voltage six per second activity in all leads.

B, Sleep tracing showing sharp wave focus in left temporal region.

diagnosis was made; this record showed a continuous very high voltage slow dysrhythmia, symmetrical and synchronous in homologous head regions. There was no evidence of the focal sharp wave activity in the left temporal area which became a dominating feature of the tracing during sleep (Fig. 4*B*).

The electrographic impression of "primary convulsogenic lesion, left temporal lobe," based upon the findings during sleep, proved to be more consistent with the character of the seizures as subsequently described in greater detail by the mother. Close questioning revealed that during her spells of "unresponsiveness and bewilderment" the patient would carry out automatic, semipurposive movements, such as fumbling with her clothes, and that at the beginning of each attack the child would turn her head and torso to the right "as if trying to look at something behind her." Obviously, this is a description of a psychomotor seizure with a right contraversive onset.

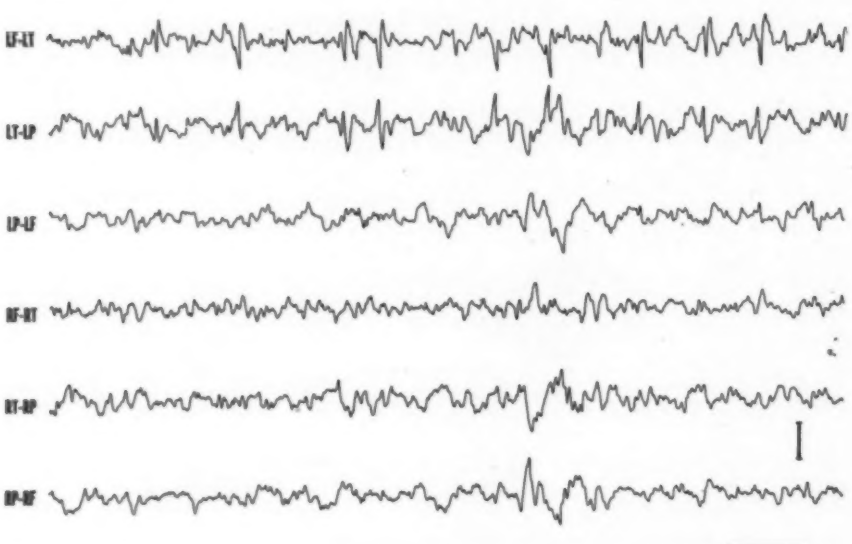


Fig. 5.—Female, aged 6½ years. Referred because of abnormal behavior and inability to talk. Temporal spike focus is revealed during sleep.

Facilitation of Recording in Handicapped, Retarded, or Uncooperative Children.—One of the outstanding values of the sleep technique is the fact that it makes possible good diagnostic tracings in children in whom it would otherwise be impossible to obtain reliable recordings. In very young or retarded children, in children who are deaf, blind, or otherwise handicapped, and, of course, in certain behavior disorders, it is frequently difficult to obtain a reliable diagnostic tracing. It is especially difficult sometimes in such cases to differentiate sharp wave and random spike activity from movement artifact. The usefulness of the sedation-sleep recording in this type of patient is clearly demonstrated by the following case. The patient, a white female 6½ years of age,

was brought for electrographic study because of abnormal behavior and inability to talk. Until the age of 3 years the child had developed normally and appeared in good health. At that time she developed a "fever blister" on her lip and was lethargic for a period of several weeks. Sometime during this episode the child lost the ability to speak and upon "recovery" from her illness became very difficult to handle because of her "wild, capricious and unpredictable behavior."

When the patient was brought to the laboratory for electroencephalographic study she proved to be so hyperactive and so intractable that it was necessary to use restraint in order to apply the electrodes. After she was placed on the bed, attempts were made to hold her attention long enough to obtain a few seconds of readable tracing but without success. It was not until she finally went to sleep that a record free enough from artifact to be reliable was obtained. As soon as the patient began to sleep, a discharging slow spike focus became clearly evident near the left temporal lead (Fig. 5) and subsequent localization revealed the origin of these discharges to be in the left (dominant) frontotemporal region in the vicinity of Broca's area.

The Various Epileptiform Patterns Encountered in Sleep.—The rapid bilateral multiple sharp wave or spike discharge which the Gibbs group have designated "the grand-mal pattern," and which had a high incidence in the adult series studied by them, was observed comparatively rarely in the present study despite a high percentage of patients with a history of generalized tonic-clonic seizures. Focal phenomena and various forms of bilaterally synchronous spike and wave patterns were, by far, the most common type of larval discharge encountered in this study regardless of the type of clinical seizure reported. An important feature of the sleep tracing is that it tends to bring out certain special characteristics of the generalized spike-wave type of pattern which provide extra information of diagnostic and therapeutic significance. Electroencephalographic study of many epileptic children has shown that for each of the several variations of this basic pattern there is a definite clinical correlate. Thus, for example, the child who shows repeated paroxysmal bursts of bilaterally synchronous three per second spike and wave complexes characterized by high voltage multiple spike discharges for each slow wave is much more likely to be subject to grand mal seizures than is the child who shows only bursts of three per second smooth-top waves or simple single spike and wave complexes. This correlation of the several forms of the basic diffuse spike and wave pattern with specific clinical states is the subject of another communication and hence it is sufficient to indicate here that, because latent components of the seizure pattern of a given patient tend to become manifest during sleep, a sleep tracing provides more information for the total assessment of the convulsive state of the patient and thus facilitates the selection of a more rational therapeutic program.

It has already been shown that sleep may reveal the classic three per second simple spike and wave pattern even when a long waking record and/or other methods of activation fail to elicit evidence of a convulsive disorder. The practical value of this activating property of sleep in children with suspected petit mal who cannot, or will not, overventilate need not be emphasized.

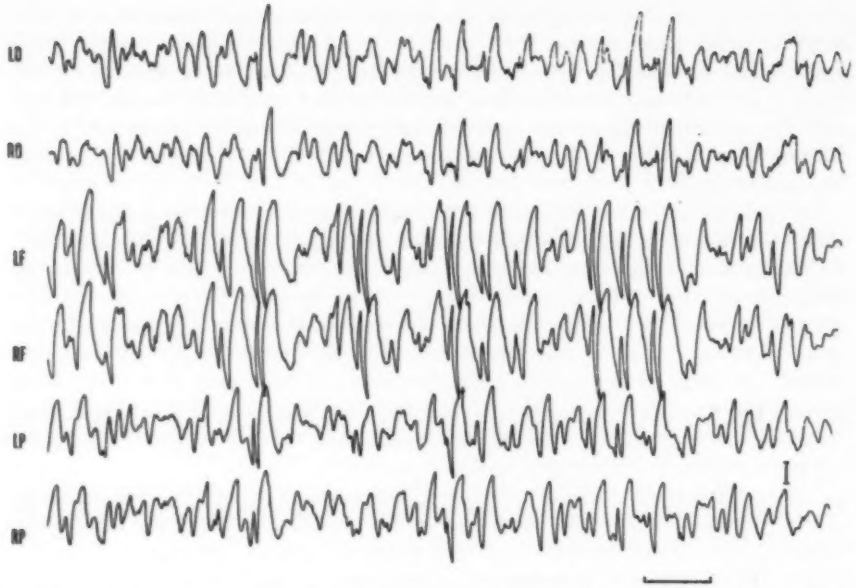


Fig. 6.—Female, aged 6½ years. Akinetic seizures involving complete loss of postural tone and momentary collapse to the floor. Generalized tonic-clonic seizures on several occasions.

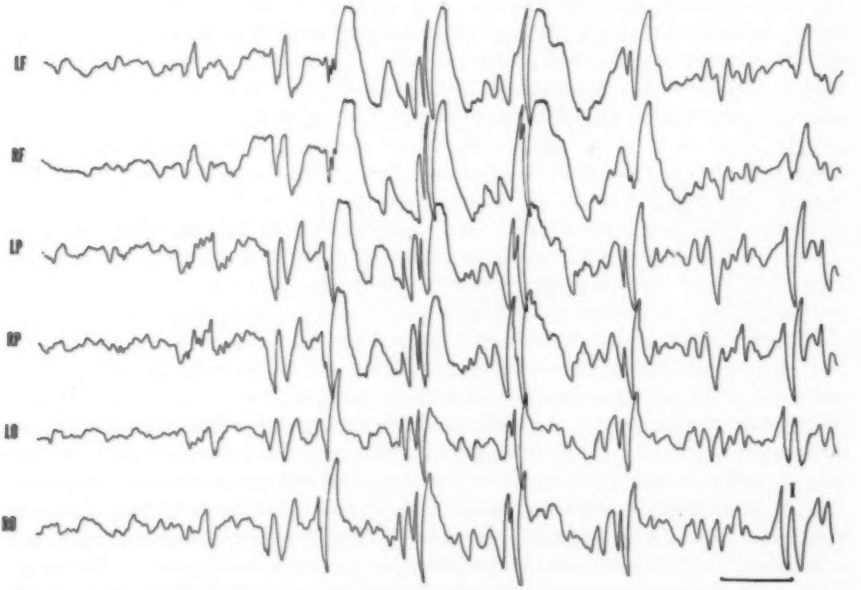
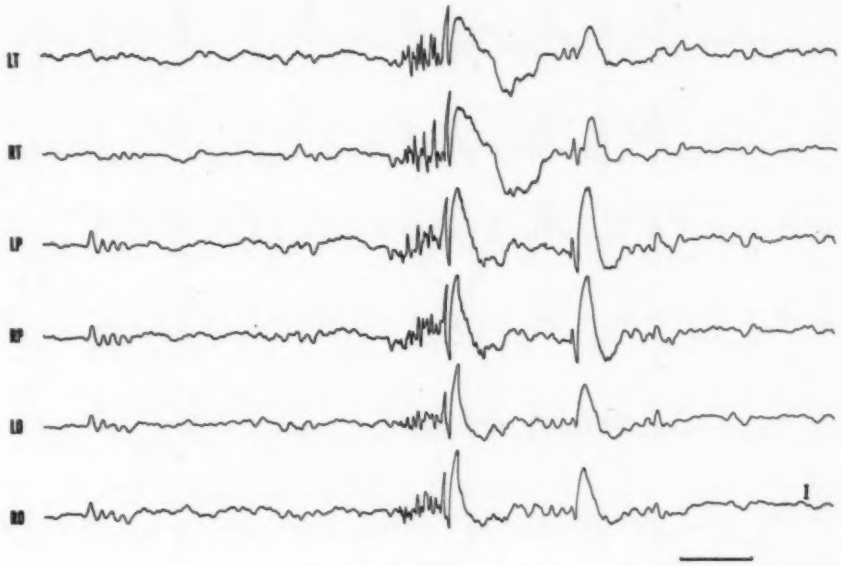


Fig. 7.—Male, aged 5½ years. Akinetic seizures consisting of simple momentary head-bobbing and in more severe attacks of a sudden bowing movement with hyperextension of the arms.



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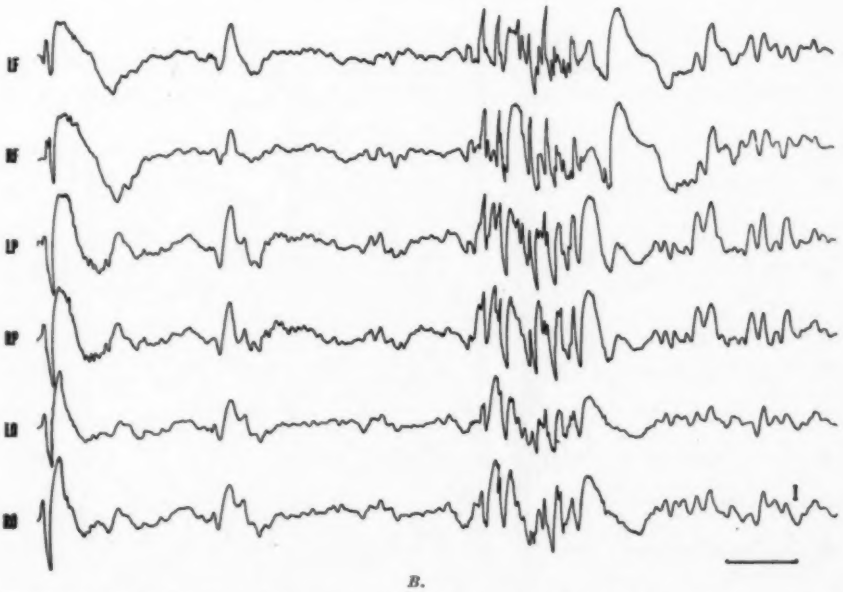

B.

Fig. 8.—*A* and *B*, Male, aged 5 years. Attacks of unconsciousness at high level, with arrest of motion. Several attacks which were described as classic grand mal type.

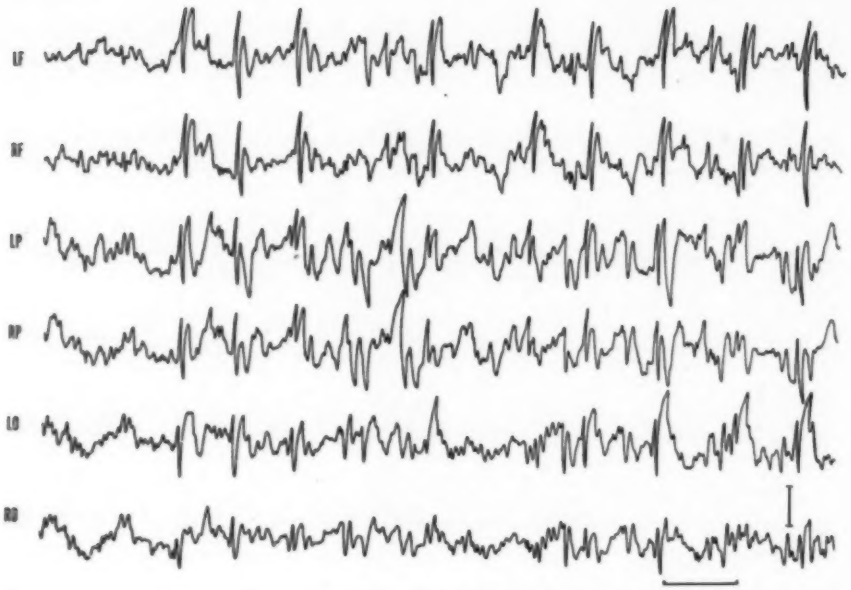

Fig. 9.—Male, aged 11 years. One "tonic convulsion" following several days of "heavy" Pyribenzamine medication for "hay fever."

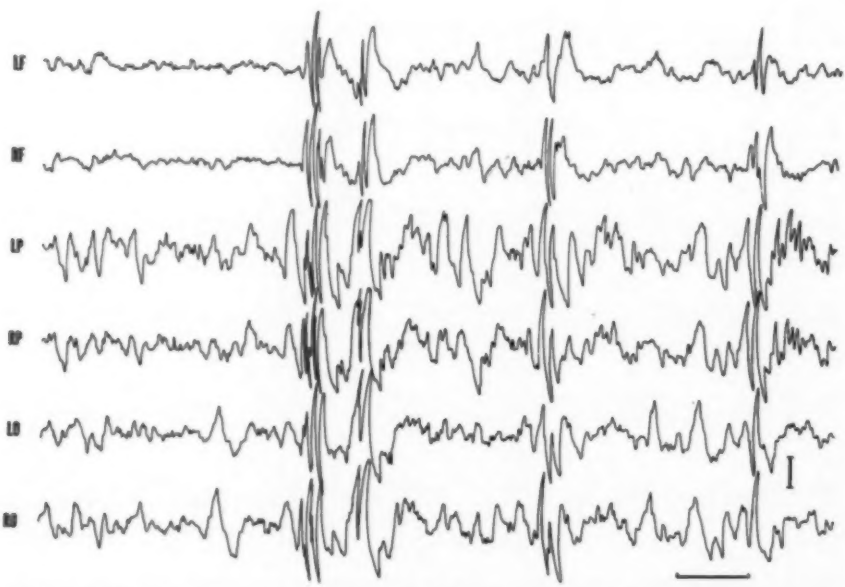

Fig. 10.—Male, aged 3 years. Serial myoclonic jerks without loss of consciousness or position.

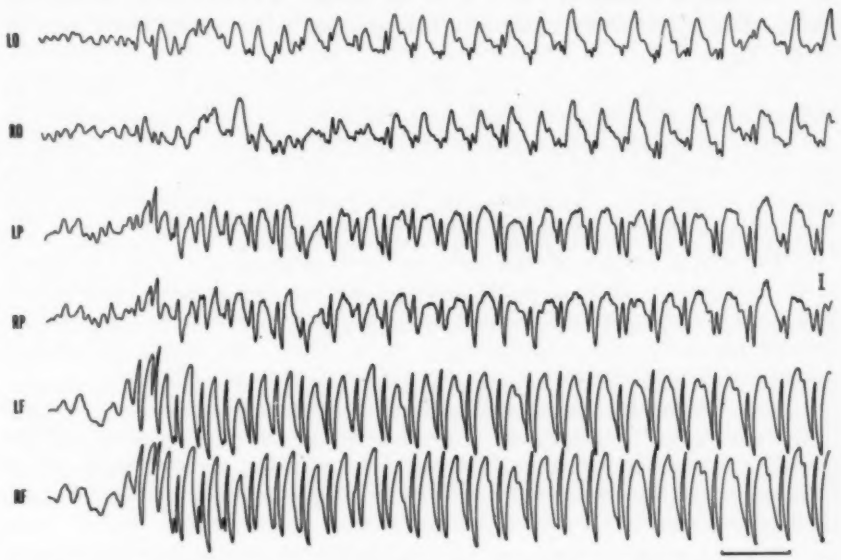

Fig. 11.—Female, aged 15 years. Generalized tonic-clonic seizures for past ten years. No petit mal-like attacks ever observed or recognized.

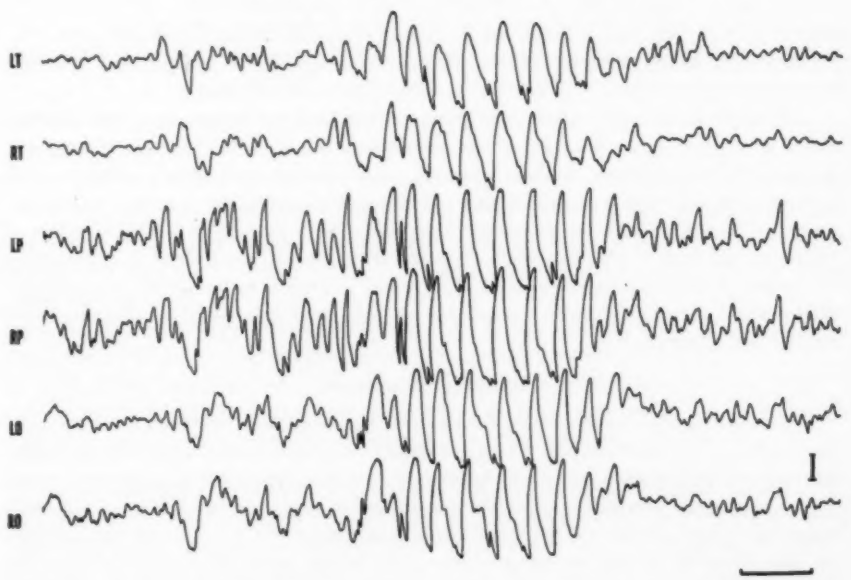

Fig. 12.—Male, aged 10 years. Numerous brief episodes during past year of elevation of the eyes toward ceiling with momentary unresponsiveness and subsequent amnesia for the period of the attack (approximately ten seconds).

The sample tracing of Fig. 2 is, as has already been shown, an example of the activating properties of sleep in bringing out latent epileptiform activity of this kind.

Fig. 6 is from a sleep tracing of a white female child 6½ years of age subject to akinetic seizures. These began with simple head-bobbing attacks at the age of 20 months and progressed through the bowing or "salaam" stage to the point when total inhibition of postural tone would occur and she would drop suddenly to the floor. No simple petit mal attacks were ever observed, but she had had generalized tonic-clonic seizures on several occasions.

The similar pattern of slow spike and wave discharges in Fig. 7 is from a sleep tracing of a white male 5½ years of age who had akinetic seizures consisting of either a simple head-bobbing or in more severe attacks of a sudden bowing movement with hyperextension of the arms. No simple petit mal or grand mal attacks were ever known to have occurred in this boy.

Figs. 8*A* and *B* are samples from a sleep recording of a 5-year-old Mexican child who during the four months previous to the time of recording had had several "attacks of unconsciousness without convulsive movements or loss of posture." He had also had two seizures in which he fell to the ground "and twitched all over."

Fig. 9 was taken from a tracing made during sleep of an 11-year-old white male who had had one convulsive episode following several days of "heavy" Pyribenzamine medication for "hay fever." The seizure was described by the parents as a "tonic spasm of the body" with unconsciousness. The eyes were rolled back in the head and the neck and torso dorsiflexed. There were no convulsive movements, and no tongue biting or incontinence. This child has had no more attacks since being placed on medication (Mebaral).

Fig. 10 shows some of the complex paroxysmal discharges recorded during sleep in a white male 3 years of age who was subject to rapid serial myoclonic jerks usually occurring without loss of consciousness and rarely with loss of posture. Sometimes a single flexor twitch of the upper extremities would occur; but in major attacks the arms, legs, and trunk seemed to be involved, and there would be a rhythmic series of jerks which caused the child's whole body to shake for three or four seconds. This child is known to have had one generalized seizure during a febrile illness but no petit mal attacks had been observed, or at least recognized.

GENERAL DISCUSSION

In adults, the various wave forms and the sequential patterns of sleep have been fairly well established[8-34] and are easily recognized with a little experience. In infants and young children, however, the electrographic patterns of sleep are much more complex and show considerable variation with age. Only one paper devoted entirely to this subject has appeared in the literature and this in the form of a "preliminary" report.[35] Much more work will have to be done with normal children before the more subtle aberrations of wave form and pattern can be differentiated. The several types of epileptiform discharge illus-

trated in this paper are easily recognized because they differ very little from their analogues of the waking state. But, while it is easy to recognize clearly epileptiform patterns in a sleep tracing, it is also easy for the inexperienced to mistake some of the normal sleep configurations of children for epileptiform activity, as evidenced by the several false impressions of children's sleep tracings in a recent communication on this subject.* Although Smith's early description[35] of the successive electrographic changes of sleep in young children is basically correct it is somewhat oversimplified. The electrical sleep patterns in children are much more complex than he originally pictured them, and there are periods of hypersynchronous activity on falling asleep, on partial arousal, and upon awakening which may resemble closely the paroxysmal bursts of idiopathic epilepsy and which may be easily mistaken for them.

In conclusion, it seems justifiable to state that the results of these studies have demonstrated that recording of a sleep tracing in convulsive patients has become a categorical imperative and that a patient can no longer be regarded as adequately examined from an electroencephalographic standpoint without it. Until some more effective method of activation is introduced it seems clear that sleep should be used routinely in all convulsive patients not showing definite diagnostic signs in the waking record. It must not be supposed, however, that a sleep tracing can replace, or be substituted for, the routine waking study, for it has been observed repeatedly that a child may show a grossly dysrhythmic record while awake and yet fail to show clearly recognizable epileptiform activity during sleep.

SUMMARY

The recently reported observation that the sleep state activates the appearance of epileptiform abnormalities in the electroencephalogram are confirmed and extended. Furthermore it is shown that the use of mildly sedative doses of Nembutal to promote sleep in children does not significantly reduce the activating properties of this state.

The routine use of sedative-induced sleep is shown to be a valuable adjunct to routine clinical electroencephalography in children for the following reasons:

1. Latent epileptiform activity not present in a waking record and not activated by such measures as hyperventilation may nevertheless become manifest during sleep.

2. A primary convulsogenic focus may be revealed in sleep when the waking record is of a type suggestive of a generalized convulsive state.

3. Sleep produced by mild sedation provides a means of obtaining diagnostic tracings in children in whom, because of mental retardation, physical handicap, or behavioral difficulties, it would not otherwise be possible.

*The tracings illustrated in the paper referred to are for the most part of such poor technical quality that it is difficult to evaluate them satisfactorily. However, several of the samples called epileptiform ("petit mal waves") by the authors are clearly examples of rhythmic slow activity which is generally seen in very young children and infants in certain stages of sleep. Tracings which are technically poor increase the likelihood of misinterpreting the high voltage and complex episodes which occur during sleep, and equipment which is capable of following the wide variations of amplitude and frequency without blocking is a necessity in the use of routine sleep in children. In this laboratory it is routine to use the very low frequency filter during some of the recording period in order to filter out some of the very slow extremely high voltage waves characteristic of deep sleep so as to visualize more clearly the other components of the pattern without excessive pen blocking and collision.

The characteristics of the various clearly abnormal electrical discharges which occur during sleep are described and discussed in relation to their clinical correlates.

REFERENCES

1. Temkin, O.: The Falling Sickness: A History of Epilepsy from the Greeks to the Beginnings of Modern Neurology, Baltimore, 1945, The Johns Hopkins Press.
2. Gibbs, F. A., and Gibbs, E. L.: Atlas of Electroencephalography, Cambridge, Mass., 1941, Lew A. Cummings Co.
3. Gibbs, E. L., and Gibbs, F. A.: Diagnostic and Localizing Value of Electroencephalographic Studies in Sleep, Res. Publ. Assoc. Nerv. Ment. Dis. **26**: 366, 1947.
4. Scott, D., and Masland, R. M.: Effect of Drug Therapy on Electroencephalograms of Epileptic Patients, Arch. Neurol. & Psychiat. **48**: 505, 1945.
5. Fuster, B., Gibbs, E. L., and Gibbs, F. A.: Pentothal Sleep as an Aid to the Diagnosis of Localization of Seizure Discharges of the Psychomotor Type, Dis. Nerv. System **9**: 199, 1948.
6. Hoefer, P., Hoff, H. H., and Pluvinage, R. I. L.: The Effect of Anticonvulsant Therapy on the Electroencephalogram of Patients With Idiopathic Epilepsy, Tr. Am. Neurol. A. **72**: 145, 1947.
7. Ulett, G.: Electroencephalograms of Dogs With Experimental Space-Occupying Intracranial Lesions, Arch. Neurol. & Psychiat. **54**: 141, 1945.
8. Bakuradze, A., and Narikasvili, S.: Spontaneous Electrical Activity of the Brain During Sleep, Tr. Beritashvili Physiol. Inst. USSR, **6**: 377, 1945.
9. Barker, W., and Burgwin, S.: Brain Wave Patterns Accompanying Changes in Sleep and Wakefulness During Hypnosis, Psychosom. Med. **10**: 317, 1948.
10. Blake, H.: Brain Potentials and Depth of Sleep, Am. J. Physiol. **119**: 273, 1937.
11. Blake, H., and Gerard, R. W.: Brain Potentials During Sleep, Am. J. Physiol. **119**: 692, 1937.
12. Blake, H., and Gerard, R. W., and Kleitman, N.: Factors Influencing Brain Potentials During Sleep, J. Neurophysiol. **2**: 48, 1939.
13. Brazier, M. A. B.: The Electrical Fields at the Surface of the Head During Sleep, EEG Clin. Neurophysiol. **1**: 195, 1949.
14. Cress, C. H., and Gibbs, E. L.: Electroencephalographic Asymmetry During Asleep, Dis. Nerv. System **9**: 2, 1948.
15. Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., and Hobart, G.: Electrical Responses of the Human Brain to Auditory Stimulation During Sleep, J. Neurophysiol. **2**: 500, 1939.
16. Davis, H., Davis, P. A., Loomis, A. L., and Harvey, E. N.: Changes in Human Brain Potentials During the Onset of Sleep, Science **86**: 448, 1937.
17. Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., and Hobart, G.: Analysis of the Electrical Response of the Human Brain to Auditory Stimulation During Sleep, Am. J. Physiol. **126**: 474, 1939.
18. Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., and Hobart, G.: A Search for Changes in Direct-Current Potentials of the Head During Sleep, J. Neurophysiol. **2**: 129, 1939.
19. Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., and Hobart, G.: Human Brain Potentials During the Onset of Sleep, J. Neurophysiol. **1**: 24, 1938.
20. Diaz-Guerrero, R., Gottlieb, J. S., and Knott, J. R.: The Sleep of Patients With Manic-Depressive Psychosis, Depressive Type, Psychosom. Med. **8**: 399, 1946.
21. Harvey, E. N., Loomis, A. L., and Hobart, G.: Cerebral States During Sleep as Studied by Human Brain Potentials, Scient. Monthly **45**: 191, 1937.
22. Henry, C. E.: Electroencephalographic Individual Differences and Their Constancy. I. During Sleep. II. During Waking, J. Exper. Psychol. **29**: 117, 1941.
23. Kakegawa, Y.: Electroencephalographic Study of Narcosis and Sleep, Acta Med. Hokkaidonensia **22**: 56, 1944.
24. Knott, J. R., Gibbs, F. A., and Henry, C. E.: Fourier Transforms of the Electroencephalogram During Sleep, J. Exper. Psychol. **31**: 465, 1942.
25. Liberson, W. T.: Problem of Sleep and Mental Disease, Digest Neurol. Psychiat. **12**: 93, 1944.
26. Liberson, W. T.: Functional Electroencephalography in Mental Disorders, Dis. Nerv. System **5**: 1, 1945.
27. Loomis, A. F., Harvey, E. N., and Hobart, G.: Potential Rhythms of the Cerebral Cortex During Sleep, Science **81**: 597, 1935.
28. Loomis, A. L., Harvey, E. N., and Hobart, G.: Further Observations on Potential Rhythms of the Cerebral Cortex During Sleep, Science **82**: 198, 1935.
29. Loomis, A. L., Harvey, E. N., and Hobart, G.: Cerebral States During Sleep as Studied by Human Brain Potentials, J. Exper. Psychol. **21**: 127, 1937.

30. Loomis, A. L., Harvey, E. N., and Hobart, G.: Distribution of Disturbance-Patterns in the Human EEG With Special Reference to Sleep, J. Neurophysiol. 1: 413, 1938.
31. Marinesco, G., Sager, O., and Kreindler, A.: Etudes Electroencephalographique. Le Sommeil Naturel et le Sommeil Hypnotique, Bull. Acad. de méd. Paris 117: 273, 1937.
32. Marinesco, G., Sager, O., and Kreindler, A.: Etudes électroencephalographiques: Le Sommeil et le Coma, Bull. Acad. de méd. de Roumanie 2: 454, 1937.
33. Müller, L. R.: Ueber bioelektrische Vorgänge im Grosshirm während des Wachens und des Schlafens, Klin. Wchnschr. 18: 1589, 1939.
34. Tucci, J. H., Brazier, M. A. B., Miles, H. H. W., and Finesinger, J. E.: A Study of Pentothal Sodium Anesthesia and a Critical Investigation of the Use of Succinate as an Antidote, Anesthesiology 10: 25, 1949.
35. Smith, J. Roy: The Electroencephalogram During Normal Infancy and Childhood: III. Preliminary Observations on the Pattern Sequence During Sleep, J. Genet. Psychol. 53: 471, 1938.

SOME PROBLEMS COMMON TO THE PEDIATRICIAN AND THE ORTHODONTIST

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INTRODUCTION

NOWADAYS the value and necessity of pediatric service are well recognized by the parents of our American children. Because of this, when economic conditions allow it, the pediatrician is a member included in the medical personnel that looks after the physical welfare of the American family unit. Parents have discovered that the practitioner of pediatrics is by disposition, training, and experience, specially qualified to administer to the physical needs of their children. With this knowledge parents place great confidence and trust in the ability of the pediatrist to treat all and cure most childhood diseases, as well as to advise them on all topics concerning the physical well-being of their children.

It is because the pediatrician has come to be considered an oracle on child health and welfare that he is ofttimes consulted about a wide range of childhood problems, many of them purely dental, and some specifically orthodontic in nature.

PURPOSE

It is my purpose to anticipate some of these questions that are asked the pediatrist about children's dental health and pose their answers from a dentist's and orthodontist's point of view.

Another purpose of this presentation is to emphasize the necessity of including an examination of the oral cavity in any so-called physical examination of the child patient. It is presumptuous to assume that an examination is complete if it neglects the mouth. While it is not reasonable to suppose that the pediatrist has the knowledge to give a thorough examination of the oral cavity, it is not unreasonable to expect him to have enough information on the structures in this area to recognize gross deformities and abnormalities. When dental anomalies are suspected, the pediatrician should refer the patient to the dentist.

CHRONOLOGY OF THE DENTITION

The most common query of a dental character that is directed to pediatricians is that concerning the eruption time of primary and/or permanent teeth of children. Parents are concerned about what they presume are abnormalities in the chronology of their children's dentition and often seek information about it.

We have known for many years that a wide range of variation is to be found in the time that several teeth erupt. Even a significant latitude exists within so-called normal limits. Many studies have been made to ascertain the average ages that the individual teeth in the primary and permanent dentitions erupt. These investigations revealed that besides age, sex and body build, among other things,

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are influencing factors. In girls, teeth erupt earlier than in boys, and tall children are dentally precocious in comparison with short children of the same chronological age.

One of the best known and most widely used tables on tooth development and eruption is that of Logan and Kronfeld as modified by McCall and Schour. The table is presented here in abbreviated form.

CHRONOLOGY OF THE HUMAN DENTITION*

Logan and Kronfeld (slightly modified by McCall and Schour)

		TOOTH	HARD TISSUE FORMATION BEGINS	ENAMEL COMPLETED	ERUPTION	ROOT COMPLETED
Primary Dentition	Maxillary	Central	4 mo. in utero	1½ mo.	7½ mo.	1½ yr.
		Lateral	4½ mo. in utero	2½ mo.	9 mo.	2 yr.
		Cuspid	5 mo. in utero	9 mo.	18 mo.	3¼ yr.
		First M.	5 mo. in utero	6 mo.	14 mo.	2½ yr.
		Second M.	6 mo. in utero	11 mo.	24 mo.	3 yr.
	Mandibular	Central	4½ mo. in utero	2½ mo.	6 mo.	1½ yr.
		Lateral	4½ mo. in utero	3 mo.	7 mo.	1½ yr.
		Cuspid	5 mo. in utero	9 mo.	16 mo.	3¼ yr.
		First M.	5 mo. in utero	5½ mo.	12 mo.	2¼ yr.
		Second M.	6 mo. in utero	10 mo.	20 mo.	3 yr.
Permanent Dentition	Maxillary	Central	3-4 mo.	4-5 yr.	7-8 yr.	10 yr.
		Lateral	10-12 mo.	4-5 yr.	8-9 yr.	11 yr.
		Cuspid	4-5 mo.	6-7 yr.	11-12 yr.	13-15 yr.
		First Bi.	1½-1 ¾ yr.	5-6 yr.	10-11 yr.	12-13 yr.
		2nd Bi.	2-2¼ yr.	6-7 yr.	10-12 yr.	12-14 yr.
		First M.	At birth	2½-3 yr.	6-7 yr.	9-10 yr.
		2nd M.	2½-3 yr.	7-8 yr.	12-13 yr.	14-16 yr.
		Third M.	7-9 yr.	12-16 yr.	17-21 yr.	18-25 yr.
	Mandibular	Central	3-4 mo.	4-5 yr.	6-7 yr.	9 yr.
		Lateral	3-4 mo.	4-5 yr.	7-8 yr.	10 yr.
		Cuspid	4-5 mo.	6-7 yr.	9-10 yr.	12-14 yr.
		First Bi.	1¾-2 yr.	5-6 yr.	10-12 yr.	12-13 yr.
		2nd Bi.	2¼-2½ yr.	6-7 yr.	11-12 yr.	13-14 yr.
		1st M.	At birth	2½-3 yr.	6-7 yr.	9-10 yr.
		2nd. M.	2½-3 yr.	7-8 yr.	11-13 yr.	14-15 yr.
		3rd. M.	8-10 yr.	12-16 yr.	17-21 yr.	18-25 yr.

*Wheeler: Textbook of Dental Anatomy and Physiology.

Your attention is called to age spread given in the eruption time of various teeth. These figures represent the average chronological age range that usually has been reached when any given primary or permanent tooth erupts. Two facts exist which should preclude the slavish use of information coming from this or any similar table:

1. The figures represent *average* ages of eruption of teeth (it is often misleading to apply *average* values to *individual* cases).

2. The chronological age of the individual may be behind, synchronous with, or in advance of his physiological age. Eruption of the teeth being an expression of biological or physiological processes, it is apparent that whether the eruption time of the teeth in any given individual case is acceptable or unacceptable depends on much more than chronological age alone.

There are acquired as well as inherited conditions that may influence eruption time of teeth. Endocrinopathies, particularly those involving the thyroid, parathyroid, or pituitary glands, are examples.

Hypothyroidism, both the congenital and acquired types, is sometimes associated with late eruption of primary teeth, retarded exfoliation of these teeth, and delayed or disturbed eruption of the permanent teeth. If hypoparathyroidism develops in infancy, there is abnormal calcium metabolism and defective calcification of teeth. In early hyperpituitarism, involving the anterior lobe, there is precocious eruption of the primary teeth, while hypopituitarism that develops early is often associated with retarded resorption of the roots of the primary teeth and late eruption of the permanent teeth.

There are many factors that cause variation in the chronology of the dentition. There is, however, a rather definite and fixed order or sequence in which the various primary and permanent teeth make their appearance in the oral cavity.

The sequence of eruption of teeth is limited to minor variations only. Disorderly eruption of teeth is symptomatic of some abnormality that is operating locally to disturb the order of tooth eruption.

It is rewarding to look for the cause or causes of the disorderly eruption of teeth because in the search other oral conditions are diagnosed that might otherwise go undiscovered and untreated. A common example will illustrate this point. A patient exhibits disorderly eruption of teeth in the maxillary incisor area in this manner: the lateral incisors have erupted and only one of the central incisors is clinically evident. Both central incisors would always be expected to appear before the lateral incisors. In looking for an explanation for this condition, it would be well to consider the likelihood that one or more supernumerary teeth are present in the central incisor area and are preventing the eruption of this tooth. Dental roentgenograms of this area in question would confirm or deny the tentative diagnosis.

These extra or supernumerary teeth are invariably a cause of trouble. Either they prevent the eruption of one or more permanent teeth or they force them to assume abnormal positions at the time of their eruption. If unerupted they may undergo cystic degeneration. There are cases recorded of dentigerous cysts originating with retained, unerupted supernumerary teeth. Early detection of these teeth followed by their prompt removal will prevent these untoward effects.

DENTAL CARIES

There are some pathological states of the hard tissues of the oral cavity that are of orthodontic and pediatric import.

Dental caries or tooth decay is the disease process most commonly found in modern civilized man. In recent years, the dental health education of our people has become so effective that most parents know the importance of preventing dental caries in their children. They have been taught that neglect of tooth decay may ultimately leave the child with an impaired or crippled masticatory apparatus. They have learned that the primary phase of the digestive process takes place in the oral cavity and that whenever this important physiological process is incompletely or inefficiently done the child's physical well-being eventually suffers in varying degrees.

When the carious lesion penetrates the enamel and dentine layers of the tooth crown, necrosis of pulpal tissue with subsequent abscess formation at the apex of the root usually follows. Such teeth may become potential foci of infection, or portals of entry for blood stream invasion by any of the types of pathogenic organisms that may be part of the bacterial flora of the oral cavity.

To avoid the necessity of crippling masticatory function by being forced to extract teeth that are broken down or abscessed through caries is the concern of informed and interested parents, the pediatrician, and the orthodontist.

DIET

Parents continually consult the pediatrician about the food elements that are necessary to include in their children's diet. More than enough emphasis has been placed on the value of having adequate amounts of calcium, phosphorus, and vitamin D in the diet to insure proper calcification of dental tissues. This has led to the false assumption that tooth decay can be avoided by having perfectly calcified teeth which in turn are developed by a diet especially well fortified with calcium, phosphorus, and vitamin D. If dental caries were a disease peculiar to poorly calcified tooth structure only, this assumption would be a valid one. Unfortunately it is not valid. Under appropriate environmental conditions, well-calcified teeth may decay as surely, though not as rapidly, as do less well-calcified teeth. The acids formed in the dental plaque as a product of bacterial activity attack the enamel and produce caries in well calcified teeth with facility.

These comments should not be interpreted to mean that we believe an adequate diet is unimportant in fostering favorable development of the masticatory apparatus. It is of great importance while the crowns of the primary and permanent teeth are forming, i.e., calcifying. Chronologically speaking, this would encompass a period from age 4 months in utero to age 8 years. Beyond 8 years of age the calcium, phosphorus, and vitamin D content of the diet is of no significance in development of the crown of the tooth.

Food prescriptions that are written containing large amounts of calcium and vitamin D or recommend the ingestion of concentrated form of these substances are irrationally used if they are intended to arrest caries or improve the quality of the teeth of a patient who is older than 8 years of age.

After eruption of the tooth there is no avenue known at present by which calcium can be brought to the enamel of the tooth crown or taken from it. However, emphasis on diet is still a practical approach to the solution of the problem of controlling dental caries at any age. Instead of emphasizing the necessity of an adequate diet to reduce tooth decay, the pediatrician should advise inquiring parents to eliminate foods of high sugar content from the child's diet. They should inform the parents that extensive dental caries can be found in the teeth of children whose diets are completely adequate in respect to vitamins, minerals, proteins, carbohydrates, fats, amino acids, and the other essential elements, if in accompaniment there is an excessive amount of refined sugar in these foods. They should be informed also that caries is not a deficiency disease. Irrefutable evidence in support of this fact is to be found today in Italy where there are

thousands of children who are practically caries free, and yet these children, born in the war years, have been reared from infancy on a near starvation diet. Adequacy or inadequacy of the diet does not influence the child's immunity or susceptibility to tooth decay; the carbohydrate content of it does.

It seems impossible to dissuade the American people from their habit of ingesting large quantities of carbohydrate. As a nation, we are eating many foods daily that contain great amounts of refined sugar.

Statistics, supplied by the United States Department of Argiculture, reveal that last year in this country the per capita consumption of sugar was more than 100 pounds. This incredible amount of carbohydrate in our diet is the explanation for the fact that today there are thirty-three million cavities in the teeth of the children of our nation and that new cavities are developing six times more rapidly than dental restorations can be inserted.

The pediatrist can render his patients a valuable service by pointing out the danger of including large quantities of concentrated sweets in the diet. The eating habits of our children can be altered in a desirable direction if the pediatrician and the dentist collaborate in this campaign of educating parents to reduce the sugar-containing foods in the child's diet.

PERNICIOUS HABITS

There is a group of perverted oral habits that interest the pediatrist and orthodontist. Many times parents consult these specialists about pernicious habits and very often conflicting opinions are given. I refer to perverted sucking habits and would include lip- and cheek-sucking in this category along with thumb- or finger-sucking.

The cause and effect of these sucking acts depend, to a great extent, upon the developmental age of the child. As Massler and Wood[1] point out, sucking habits are perfectly normal acts in infancy. They may be signs of fatigue or a symptom of retarded emotional development in the younger child, while in the older child they may indicate emotional and social immaturity.

We will all agree that sucking of any and all types is a normal and desirable activity in the infant. It is an instinctive act that is necessary for the preservation of life in all mammalian forms.

According to Shaffer,[2] the infant will suck on any object that is brought into contact with the lips and this reflex behavior lasts for the first several months of postnatal life. For this reason thumb- or finger-sucking in infancy may be disregarded. It becomes an act of some import when it is continued and practiced excessively, because then it may displace the incisor teeth and the premaxillary portion of the maxilla as well as restrain the normal forward growth of the mandible.

However, at this early age, the possibility of a deformity of the dentofacial complex developing from the perverted sucking habit is of less significance than the fact that this type of sucking indicates the child is (a) incompletely nourished, (b) inadequately loved, or (c) insufficiently rested. Therefore, the sucking can usually be controlled or eliminated by supplying more food, more affection, or more rest. The parents should be advised of this by the pediatrician.

Unscheduled feeding has eliminated most of the sucking which started because the infant was hungry. The practice of regularly scheduled feeding periods, rigidly followed, has largely given away to the policy of feeding the child whenever he is hungry and letting him eat as much as he wants. This has prevented many perverted sucking habits from developing.

Parents should also be told that the infant needs the manipulation that comes at feeding time. The bottle holder may be an accessory that gives the mother more time for her household duties, away from the baby's crib, but it is not conducive to a normal psychobiological development of the infant. There are many cases of perverted thumb-sucking that have been satisfactorily treated by advising the parents to fondle and cuddle the baby more.

Most pernicious sucking habits are discontinued by the time the child is 2 years old. The preschool child who occasionally sucks his thumb before going to sleep should not concern us. If the act is not practiced sporadically but continuously throughout the day, Massler and Wood[1] believe that it is a symptom of emotional maladjustment or rejection. In this case the habit is symptomatic of some psychological difficulty which should be corrected rather than making an effort to break the habit.

Infrequent thumb- or finger-sucking has no deleterious effect on the primary dentition. If the act is practiced often and with vigor, it may affect the positions of the primary anterior teeth and the shape of the premaxillary process. Whenever the cause of the sucking act can be discovered and successfully treated, the malpositions of the primary dental arch are self-correcting. Lewis[2] observed that in all cases in which the thumb-sucking habit was discontinued by the sixth year, the dental malformation corrected itself without appliances.

Thumb-sucking which is continued beyond the age of 6 years cannot be taken lightly, because it indicates a gross social and emotional maladjustment. The effects on the denture are more serious too. The patient develops an "open bite." These patients almost invariably become indications for orthodontic mechanotherapy.

It is because the orthodontist has many opportunities to see the damage wrought on the dentofacial complex by perverted sucking habits that he is seldom casual about these habits. All orthodontic practitioners, even the inexperienced, have seen and have been required to treat malocclusions that could have been prevented if proper interceptive therapy had been applied at an earlier date.

The correction of perverted oral habits requires that the pediatrician and the orthodontist work in concert. They should consider those patients 2½ years of age or older who are continuous thumb-suckers worthy of examination and study. The pediatrician may find that the cause of the act is insufficient nutrition or rest, an unfavorable social climate in the home, or inadequate parentage. If correction of these deficiencies does not result in discontinuance of the habit, the orthodontist should be consulted to design an appropriate appliance for the correction.

The most satisfactory form that the appliance may take is an intraoral device specially fabricated for the individual case. If such an appliance is to be used,

it is important that the orthodontist make the patient feel that he is not being chastised with the appliance. Hughes[4] feels that unless the child can comprehend that the orthodontist is doing work of direct benefit to his personal welfare, he is likely to become uncooperative and resistant. Therefore, Hughes recommends that the patient be given a little explanation and education of what is being done for him.

In conclusion, it should be emphasized that perverted sucking habits are usually symptoms of emotional disturbance and therefore our greatest attention should be directed to the child rather than the pernicious act.

SUMMARY

1. The pediatrician is often quizzed on dental and orthodontic subjects; therefore, he should have some information of them.

2. A complete physical examination, worthy of the designation, should not overlook the oral cavity.

3. Wide variations, within a normal range, exist in the average age of eruption of the various primary and permanent teeth.

4. Sex, body build, and the endocrines, among other things, influence the chronology of the dentition.

5. Neglect of caries in the primary or permanent dentitions is unwise because this policy cripples masticatory function and may make the teeth foci of infection.

6. To reduce tooth decay, dietary control with the reduction of foods containing refined sugar should be encouraged by the pediatrician and the dentist.

7. Thumb-sucking may become a habit that concerns the pediatrician and the orthodontist. The pediatrician is involved because if the act is practiced continuously by a child who is older than 2½ years of age, it indicates emotional maladjustment or rejection which requires treatment. The orthodontist is involved because it is wise to intercept perverted sucking habits early. Intraoral appliances are the best interceptive devices. If the sucking habits persist beyond the age of 6 years, a permanent dentofacial anomaly results.

REFERENCES

1. Massler, Maury, and Wood, Arthur: Thumb-Sucking, J. Dent. Child. **16**: 1, 1949.
2. Shaffer, L. F.: Psychology of Adjustment, Cambridge, 1936, Houghton Mifflin Co., pp. 32-40.
3. Lewis, Samuel J.: Habits Influencing the Deciduous Dentition, J. Am. Dent. A. **18**: 1766, 1931.
4. Hughes, Byron O.: The Growth of Children—Psychological and Hereditary Factors, Am. J. Orthodontics **35**: 16, 1949.

GROWTH AND DEVELOPMENT OF NEGRO INFANTS

III. Growth During the First Year of Life as Observed in Private Pediatric Practice

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INTRODUCTION

IT HAS often been reported in the literature that Negro infants grow slower in height and weight than white infants.[1-4] Some workers[3, 5] believe that separate standards of growth are necessary for the two races. Many reasons have been given for this apparent difference in growth. Some writers[2, 6] have stressed environmental socioeconomic factors, while others[1, 5] have emphasized racial differences on the basis of physical anthropology.

With the exception of the study by Bakwin and Patrick,[7] other surveys on the growth of Negro infants have dealt largely with indigent or dispensary material. We therefore thought it worth while to analyze the growth records of 654 Negro infants from private practice. These infants were from families in the lower middle class.

METHOD OF STUDY

This data was obtained from infants observed in private practice during the period 1940 to 1947. These infants were weighed at monthly intervals, and body length was recorded every three months (at 1, 3, 6, 9, and 12 months of age). Each infant was under observation throughout the first year of life even though some did not have perfect monthly attendance. Premature infants (infants weighing less than 2,500 grams) and those suffering from severe illnesses or major congenital deformities were excluded. These 654 infants were selected from the private practices of three pediatricians, who supervised their medical care in their respective offices throughout the first year of life. The great majority of these infants were fed breast milk and/or diluted evaporated milk with added carbohydrate. Accessory vitamins and solid foods were prescribed according to the patient's indication and the plan of the individual physician.

RESULTS AND COMMENT

We have established growth curves for the first year of life on 654 Negro infants observed in private pediatric practice. These infants were from families in the lower middle income level. Except for the report of Bakwin and Patrick, we know of no similar study on Negro infants from private practice. Bakwin and Patrick recorded weight curves alone but did not include growth in height.

From the Department of Pediatrics of Howard University School of Medicine and the Pediatric Service of Freedmen's Hospital.

TABLE I. WEIGHT IN POUNDS OF NEGRO FEMALE AND MALE INFANTS IN OUR SERIES TAKEN MONTHLY FROM BIRTH TO 12 MONTHS OF AGE

	FEMALES					MALES				
AGE IN MONTHS	WEIGHT (LB.) MEAN	STANDARD DEVIATION	STANDARD ERROR OF THE MEAN	NO. OF CASES	RANGE	MEAN	STANDARD DEVIATION	STANDARD ERROR OF THE MEAN	NO. OF CASES	RANGE
Birth	7.202	0.940	0.0528	318	5.5-10.49	7.655	1.020	0.0571	320	5.5-10.99
1	8.565	1.280	0.0823	243	6.0-14.99	8.962	1.300	0.0827	248	5.5-13.49
2	10.283	1.385	0.0809	294	7.0-15.99	10.880	1.565	0.0940	288	7.0-16.49
3	12.061	1.485	0.0850	306	8.0-17.49	12.890	1.690	0.0966	307	8.0-19.00
4	13.670	1.685	0.0978	298	9.0-23.50	14.655	1.840	0.10623	301	9.0-26.00
5	15.130	1.735	0.1002	301	10.5-23.50	16.145	1.765	0.1006	309	11.0-25.49
6	16.335	1.970	0.1134	303	11.5-25.99	17.515	1.875	0.1090	297	12.5-26.49
7	17.450	2.180	0.1278	292	12.5-28.99	18.573	1.915	0.1110	299	13.0-29.49
8	18.410	2.280	0.1328	296	13.0-30.50	19.610	2.030	0.1188	293	14.5-30.50
9	19.285	2.340	0.1396	282	14.5-30.50	21.009	2.165	0.1256	298	15.0-30.49
10	20.085	2.620	0.1595	271	14.0-32.99	21.263	2.190	0.1316	278	16.0-31.99
11	20.790	2.545	0.1575	262	15.5-34.44	22.010	2.220	0.1331	279	16.5-31.99
12	21.330	2.300	0.1426	261	15.5-28.49	22.587	2.245	0.1316	292	16.5-31.99

TABLE II. HEIGHT IN INCHES OF NEGRO FEMALE AND MALE INFANTS IN OUR SERIES TAKEN ON THE FIRST, THIRD, SIXTH, NINTH, AND TWELFTH MONTHS

	FEMALES					MALES				
AGE IN MONTHS	HEIGHT (INCHES) MEAN	STANDARD DEVIATION	STANDARD ERROR OF THE MEAN	NO. OF CASES	RANGE	MEAN	STANDARD DEVIATION	ERROR OF THE MEAN	NO. OF CASES	RANGE
1	20.873	0.808	0.0637	162	19.50-23.49	21.092	0.973	0.0746	171	19.50-23.74
3	23.297	1.023	0.0711	208	20.50-26.49	23.562	1.150	0.0794	211	20.50-26.49
6	25.989	1.018	0.0689	219	23.00-29.99	26.529	1.105	0.0756	215	23.25-29.49
9	27.903	1.093	0.0770	202	25.50-31.24	28.302	1.063	0.0720	219	25.75-31.99
12	29.447	1.090	0.0763	205	26.00-32.99	29.807	1.080	0.0732	219	26.25-32.99

Weight and Height for Male and Female Infants in Our Study.—The growth in weight and height of the infants in our study during the first year of life is demonstrated in Tables I and II and Figs. 1 and 2. The mean birth

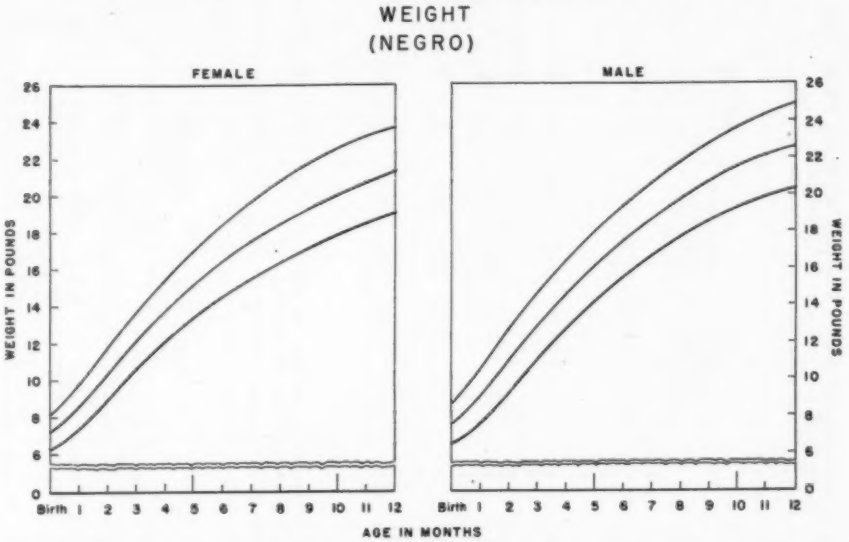


Fig. 1.—Weight in pounds from birth to 12 months of age (our report). The middle curve is the mean weight and the two extreme curves plus or minus one standard deviation.

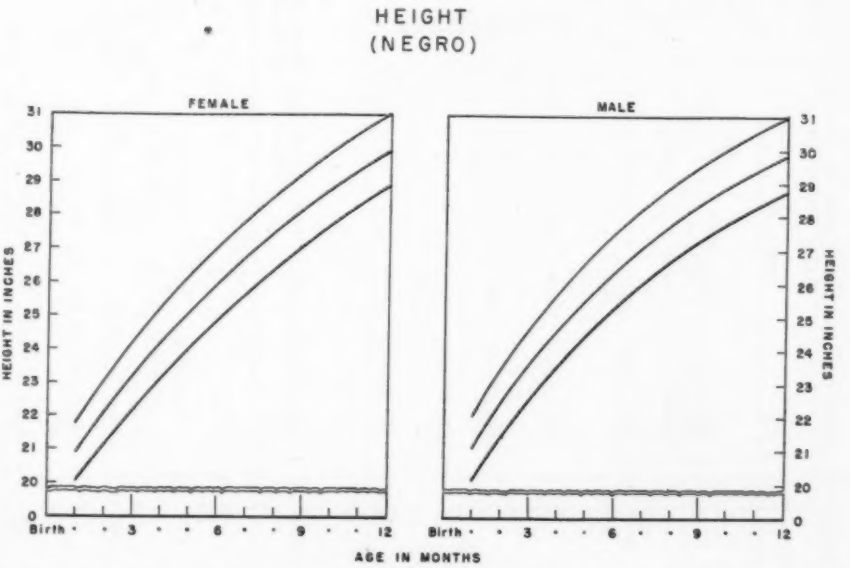


Fig. 2.—Height in inches from 1 to 12 months of age (our report). The middle curve is the mean height and the two extreme curves plus or minus one standard deviation.

TABLE III. COMPARISON OF THE WEIGHT IN POUNDS FROM BIRTH TO 12 MONTHS OF AGE OF FEMALE AND MALE NEGRO INFANTS IN OUR SERIES WITH SIMILAR DATA OF WOODBURY, MICHELSON, AND BAKWIN AND PATRICK

	FEMALES								MALES							
	WOODBURY 1918-1919		MICHELSON 1935-1936		BAKWIN PATRICK 1944		SCOTT CARDOZO SMITH 1940-1947			WOODBURY 1918-1919		MICHELSON 1935-1936		BAKWIN PATRICK 1944		SCOTT CARDOZO SMITH 1940-1947	
AGE IN MONTHS	NUMBER OF CASES	MEAN	NUMBER OF CASES	MEAN	NUMBER OF CASES	MEAN	NUMBER OF CASES	MEAN	AGE IN MONTHS	NUMBER OF CASES	MEAN	NUMBER OF CASES	MEAN	NUMBER OF CASES	MEAN	NUMBER OF CASES	MEAN
Birth			449	6.82			318	7.20	Birth			480	7.26			320	7.66
1					39	8.14	243	8.57	1					40	8.58	248	8.96
2							294	10.28	2							288	10.88
3	201	9.46	1138	8.58	57	11.88	306	12.06	3	203	10.12	1085	9.02	54	13.20	307	12.89
4							298	13.67	4							301	14.66
5					48	15.18	301	15.13	5					46	16.28	309	16.15
6	254	13.42	652	13.64			303	16.34	6	231	14.52	553	14.74			297	17.52
7					55	17.38	292	17.45	7					46	18.48	299	18.57
8							296	18.41	8							293	19.61
9	179	14.96	407	16.72	45	19.58	282	19.29	9	173	16.72	350	18.04	48	20.35	298	21.01
10							271	20.09	10							278	21.26
11					58	20.68	262	20.79	11					48	22.22	279	22.01
12	167	17.38	212	19.14	50	22.00	261	21.33	12	146	18.48	210	20.68	45	23.10	292	22.59

TABLE IV. COMPARISON OF THE HEIGHT IN INCHES FROM BIRTH TO 12 MONTHS OF AGE OF FEMALE AND MALE NEGRO INFANTS IN OUR SERIES WITH SIMILAR DATA OF WOODBURY AND MICHELSON

	FEMALES						MALES					
	WOODBURY 1918-1919		MICHELSON 1935-1936		SCOTT SMITH CARDOZO 1940-1947			WOODBURY 1918-1919		MICHELSON 1935-1936		SCOTT SMITH CARDOZO 1940-1947	
AGE IN MONTHS	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN	AGE IN MONTHS	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN
1					162	20.9	1					171	21.1
3	201	21.5	70	22.1	208	23.3	3	203	21.9	82	22.4	211	23.6
6	254	24.2	82	25.2	219	26.0	6	231	24.7	73	25.1	215	26.5
9	179	26.0	68	26.9	202	27.9	9	173	26.2	47	27.6	219	28.3
12	167	27.1	41	28.3	205	29.5	12	146	27.6	41	28.7	219	29.8

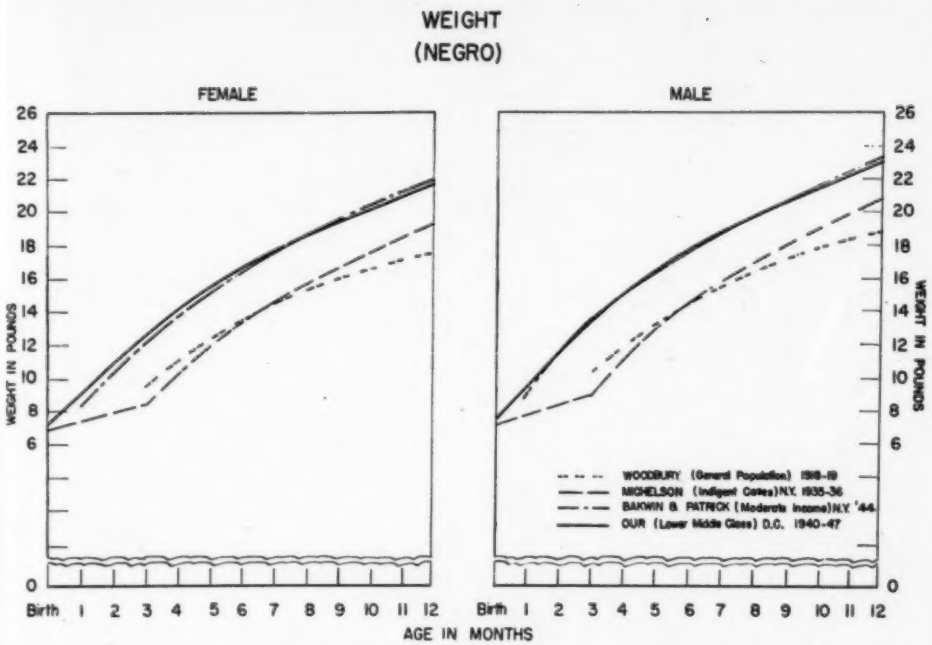


Fig. 3.—Comparison of the mean weight in pounds from birth to 12 months of age of female and male infants in our series with similar data on Negro infants from the series of Woodbury, Michelson, and Bakwin and Patrick.

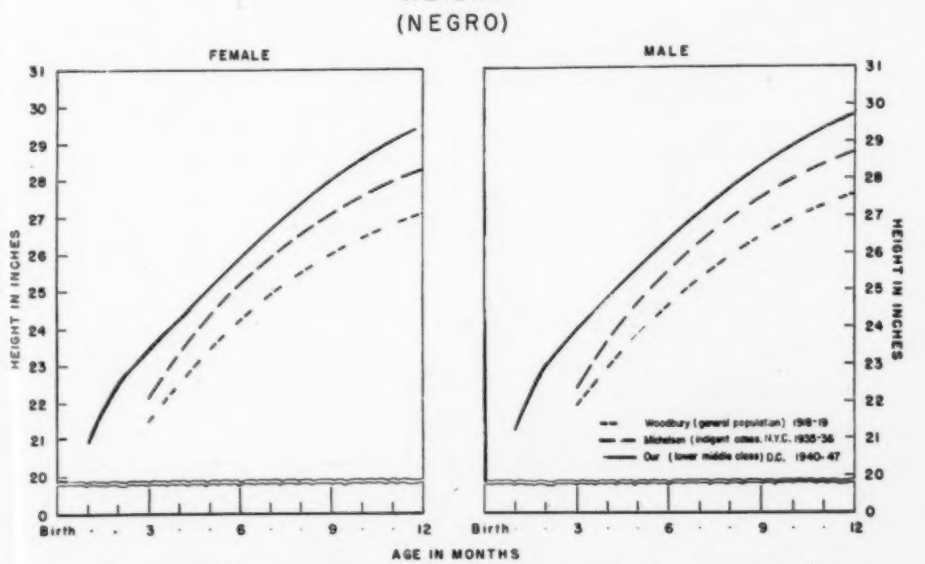


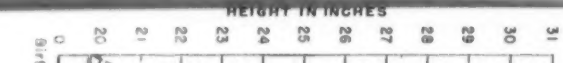
Fig. 4.—Comparison of the mean height in inches from 1 to 12 months of age of female and male infants in our series with similar data on Negro infants from the series of Woodbury and Michelson.

TABLE V. COMPARISON OF THE WEIGHT IN POUNDS FROM BIRTH TO 12 MONTHS OF AGE OF FEMALE AND MALE NEGRO INFANTS IN OUR SERIES WITH SIMILAR DATA ON WHITE INFANTS OF WOODBURY, STUART, AND DEEM

FEMALES									MALES								
	WOODBURY 1918-1919		STUART 1934		DEEM 1944		SCOTT CARDOZO SMITH 1940-1947			WOODBURY 1918-1919		STUART 1934		DEEM 1944		SCOTT CARDOZO SMITH 1940-1947	
AGE IN MONTHS	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN	AGE IN MONTHS	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN
Birth			63	744		7.50	318	7.20	Birth			50	7.63		7.75	320	7.66
2							294	10.28	2							288	10.88
3	3534	10.56	69	12.19		12.38	306	12.06	3	3780	11.22	51	12.88		13.13	307	12.89
4							298	13.67	4							301	14.66
6	5327	14.08	58	16.31		16.31	303	16.34	6	5498	15.18	44	17.07		17.31	297	17.52
8							296	18.41	8							293	19.61
9	5389	16.94	53	19.25		19.50	282	19.29	9	5509	18.04	42	20.07		20.50	298	21.01
10							271	20.09	10							278	21.26
12	5243	18.70	47	21.81		22 25	261	21.33	12	5512	20.02	38	22.19		23.25	292	22.59

TABLE VI. COMPARISON OF THE HEIGHT IN INCHES FROM BIRTH TO 12 MONTHS OF AGE OF FEMALE AND MALE NEGRO INFANTS IN OUR SERIES WITH SIMILAR DATA ON WHITE INFANTS OF WOODBURY, DEEM, AND STUART

FEMALES									MALES								
	WOODBURY 1918-1919		DEEM 1944		STUART 1934		SMITH CARDOZO SCOTT 1940-1947			WOODBURY 1918-1919		DEEM 1944		STUART 1934		SCOTT CARDOZO SMITH 1940-1947	
AGE IN MONTHS	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN	AGE IN MONTHS	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN	NO. OF CASES	MEAN
Birth					63	19.8			Birth					50	19.9		
1							162	20.9	1							171	21.1
3	3534	22.3		23.2	69	23.3	208	23.3	3	3780	22.8		23.8	50	23.9	211	23.6
6	5327	24.6		25.7	58	25.7	219	26.0	6	5498	25.3		26.5	44	26.4	215	26.5
9	5389	26.5		27.5	54	27.6	202	27.9	9	5509	27.1		28.0	42	28.1	219	28.3
12	5243	27.9		29.1	49	29.1	205	29.5	12	5512	28.5		29.7	38	29.8	219	29.8



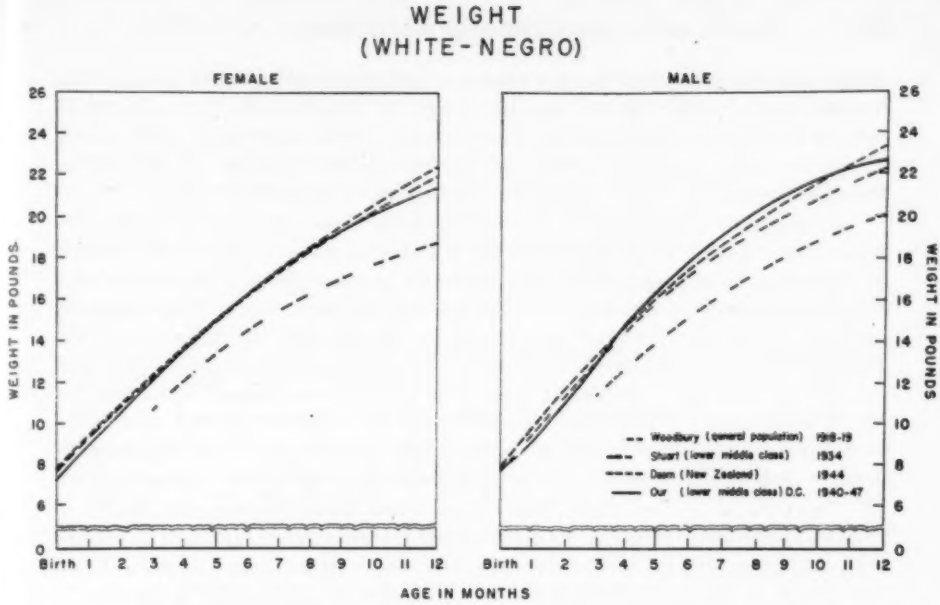


Fig. 5.—Comparison of the mean weight in pounds from birth to 12 months of age of female and male infants in our series (Negro) with similar data on white infants from the series of Woodbury, Stuart, and Deem.

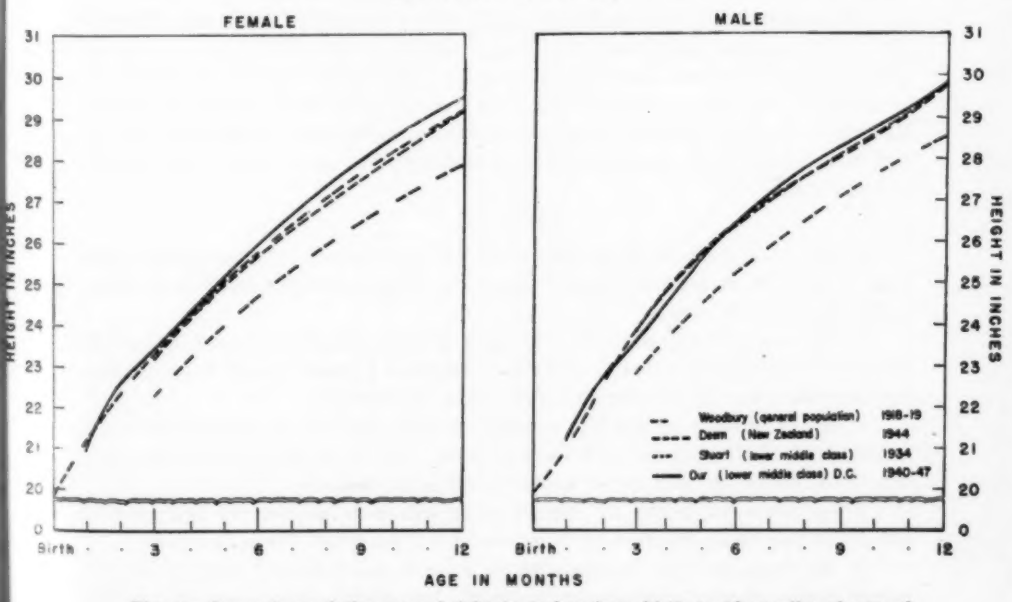


Fig. 6.—Comparison of the mean height in inches from birth to 12 months of age of female and male infants in our series (Negro) with similar data on white infants from the series of Woodbury, Stuart, and Deem.

weight for the male and female newborn infants were 7.66 pounds and 7.20 pounds, respectively. At 12 months of age the weights attained were 22.59 pounds for males and 21.33 pounds for females. The mean height at 1 month of age for males was 21.1 inches and for females 20.9 inches. At 12 months the mean height for males was 29.8 inches and for females 29.5 inches.

Comparison of Infants in Our Series With Other Reports on Negro Infants.—In Tables III and IV and Figs. 3 and 4 we have compared the growth of infants in our series with data reported by Woodbury,[8] Michelson, and Bakwin and Patrick. In Fig. 3 it is noted that our infants and those reported by Bakwin and Patrick maintained superior weight gain throughout the first year of life when compared with those of Woodbury and Michelson. In Fig. 4 the rate of increase in height of infants in our series surpassed that recorded by Woodbury and Michelson. We attribute the superior growth of infants in our series and the findings of Bakwin and Patrick to recent advances in general pediatric care and to a more favorable economic status of the families.

Comparison of Our Data With Reports on White Infants.—In Tables V and VI and Figs. 5 and 6 we have compared the growth of infants in our series with that of reports on white infants by Woodbury, Stuart,[9] and Deem.[10] From the figures it is evident that except for Woodbury's report there is no significant difference between the growth curves of Negro infants and white infants from comparable socioeconomic levels during the first year of life.

The discrepancy between the data of Woodbury (1918-1919) and current observations on growth may be attributed in part to improved methods of maternal and child care and to newer knowledge in nutrition.

The length (height) of infants in our series represented recumbent vertex-sole measurements taken with the subject stripped and lying on a pediatric table equipped with an anthropometric scale and a sliding metal bar designed to maintain the soles at right angle with the extended legs. Similarly Deem, Michelson, Stuart, and Woodbury established recumbent lengths by use of anthropometers which varied somewhat in design but gave results comparable to our method.

SUMMARY

1. We have established growth curves for the first year of life on 654 Negro infants observed in private pediatric practice. These infants were from families in the lower middle class.

2. The mean birth weight for the male and female infants was 7.66 pounds and 7.20 pounds, respectively. The mean length at 1 month of age for male and female infants was 21.1 inches and 20.9 inches, respectively.

3. At 12 months of age the weights attained were 22.59 pounds for male infants and 21.33 pounds for female infants. At 12 months of age the mean height for males was 29.8 inches and 29.5 inches for females.

4. So far as we know, our report on growth in height for the first year of life is the first to be reported on Negro infants from middle-class families.

5. We compared our results with data on Negro infants from various economic levels (general population, indigent, low middle class) reported in the

literature. The infants in our study and those reported by Bakwin and Patrick surpassed those of other series in growth throughout the first year of life. A significant difference in growth was observed when indigent infants were compared with infants from middle class levels.

6. We also compared our data with similar reports on the growth of white infants. There was no significant difference between the growth curves of Negro and white infants from comparable economic levels.

We are indebted to Dr. Howard H. Long, Associate Superintendent of Educational Research, Public Schools, Washington, D. C., for valuable aid in the analysis of the statistical data incorporated in this report.

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REFERENCES

1. Dodge, C. T. J.: Weight of Colored Infants, Am. J. Phys. Anthropol. **10**: 337, 1927.
2. Royster, L. T.: Body Type of Negro Children, Arch. Pediat. **53**: 259, 1936.
3. Bakwin, H., and Bakwin, R. M.: Studies in the Growth and Development of Children, New York State J. Med. **40**: 89, 1940.
4. Michelson, N.: Investigation in the Physical Developments of Negroes; I. Stature, Am. J. Phys. Anthropol. **1**: 191, 1943.
5. Brown, Estelle W., Lyon, R. A., and Anderson, Nina A.: Causes of Prematurity. Influence of Maternal Illness on Incidence of Prematurity. Employment of New Criterion of Prematurity for Negro Race, Am. J. Dis. Child. **70**: 314, 1945.
6. Michelson, N.: Studies in the Physical Developments of Negroes; II. Weight, Am. J. Phys. Anthropol. **1**: 289, 1943.
7. Bakwin, H., and Patrick, J.: The Weight of Negro Infants, J. PEDIAT. **24**: 405, 1944.
8. Woodbury, Robert M.: Statures and Weights of Children Under 6 Years of Age, Children Bureau Publication No. 87, LB3423A2A5 (Congressional Library), 1921.
9. Stuart, H. C.: Standards of Physical Development for Reference in Clinical Appraisement, J. PEDIAT. **5**: 194, 1934.
10. Deem, H., and Silverstone, H.: The Growth of New Zealand Infants During the First Year of Life, New Zealand M. J. **43**: 9, 1944.

THE INCIDENCE OF A NORMAL SPINAL FLUID IN ACUTE POLIOMYELITIS

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WITH the increase in the incidence of poliomyelitis during the past few years there has arisen considerable confusion in regard to the criteria necessary to make a definite diagnosis of this disease. This especially refers to the findings in the cerebrospinal fluid. Although it is known that indisputable cases of poliomyelitis do occur with a normal cytology, many physicians and some hospitals do not report cases as poliomyelitis unless evidence of the disease being present is manifested by either paralysis or increase in the spinal fluid cell count or both. During the first week of the disease, however, weakness in an extremity or muscle group is more often present than paralysis. Van Rooyen and Rhoades[1] make the statement in their book that a case can scarcely be accepted as preparalytic poliomyelitis unless the cell count is at least 12 per cubic millimeter.

On the other hand, Kolmer, Freese, Motsunami, and Meine[2] in their report of the 1916 epidemic in Philadelphia state that 23 per cent of their 609 cases had less than 12 cells in the spinal fluid. Meals and Bower[3] found in the 1930 epidemic in Southern California that 12.86 per cent of their 350 cases had negative cytology although the patients showed characteristic neurological findings. The average case in their series was admitted to the hospital on the fourth day of illness. Conway and Bigwood[4] in an epidemic of 350 cases in New York State in 1944 found that, although there was a tendency to rely heavily on the abnormalities of the spinal fluid to make a diagnosis, 48 or 10.8 per cent of the patients had a normal spinal fluid cell count and only 9 of the 48 patients were nonparalytic.

In the present study I wish to report the spinal fluid findings in 320 cases of poliomyelitis.

MATERIAL

The 320 patients reported in this study were admitted to the Geisinger Memorial Hospital from June, 1944, through December, 1949. The number of patients admitted each year is shown in Table I. The criteria followed in making a tentative diagnosis of acute poliomyelitis at the time of admission included a history compatible with the disease, fever, stiffness of the neck and/or back, spasm of the hamstrings, and evidence of central nervous system involvement with demonstrable muscle weakness or paralysis. A spinal tap was then carried out and if an abnormal cytology and/or an increase in the protein were present in the spinal fluid, further confirming the clinical diagnosis, the case was re-

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ported as poliomyelitis and treated as such. A cell count of 10 or above and a protein of 60 mg. or more were considered abnormal. However, if the spinal fluid was normal in both cell count and protein the patient was kept under observation for several days. If the clinical signs of poliomyelitis persisted and definite weakness or paralysis of one or more muscles was observed during this period a diagnosis of poliomyelitis was made.

TABLE I. PATIENTS WITH POLIOMYELITIS ADMITTED TO THE HOSPITAL FROM JUNE, 1944, THROUGH DECEMBER, 1949

YEAR	TOTAL CASES	SPINAL FLUID			
		INCREASED CELL COUNT AND/OR INCREASED PROTEIN		NORMAL CELL COUNT NORMAL PROTEIN	
		NO.	PER CENT	NO.	PER CENT
1944	41	41	100	0	0
1945	15	12	80	3	20
1946	16	16	100	0	0
1947	64	60	93.6	4	6.3
1948	80	68	85	12	15
1949	104	80	77	24	23
Total	320	277	86.2	43	13.8

Sixty-four of the 320 patients failed to show an increase in the cell count and/or increase in the protein in the spinal fluid recovered from the first spinal tap. Eight of the 64 patients were admitted from the third to the sixth week of their illness and the spinal fluid findings were not considered significant. Of the remaining 56 patients, 22 had a repeat spinal tap done within twenty-four to forty-eight hours, and 13 of these or 60.8 per cent showed an increase in cells and/or increase in the protein in the second sample of the spinal fluid. That left 43 patients or 13.8 per cent of the total number with normal spinal fluid findings and definite evidence of poliomyelitis.

TABLE II. TYPES OF CASES HAVING NORMAL SPINAL FLUID

YEAR	NONPARALYTIC	SLIGHT PARALYSIS	MODERATE PARALYSIS	SEVERE PARALYSIS	SPINOBULBAR
1945	0	1	1	0	1
1946	0	0	0	0	0
1947	0	2	2	0	0
1948	1	6	4	1	0
1949	4	10	8	2	0
Total	5	19	15	3	1

In Table II may be seen the type of case having a normal spinal fluid. Five cases were classified as nonparalytic or those who had entirely recovered from any weakness of the muscles at time of discharge from the hospital at the end of the fourteen-day quarantine period. This group is small as those cases with transitory neurological signs were not diagnosed as poliomyelitis unless cytologic changes in the spinal fluid were present. Nineteen patients had slight paralysis, 15 moderate paralysis, and 3 severe paralysis. One was a spinobulbar case. None of the patients died. Twenty-nine of the patients had involvement of the muscles of one or both legs, 3 one or both arms, 5 one arm and one leg,

4 the back, 1 the abdomen, and 1 the abdomen and left leg. All of these patients were carefully followed after discharge from the hospital. The final results are shown in Table III. At the end of three months, 22 or 51.1 per cent had completely recovered, 15 or 34.9 per cent still had some residual weakness, and 6 or 14 per cent had severe paralysis.

TABLE III. THREE MONTHS FOLLOW-UP OF PATIENTS WITH NORMAL SPINAL FLUIDS

TOTAL NUMBER	COMPLETE RECOVERY	RESIDUAL PARALYSIS	SEVERE PARALYSIS
43	22 (51.1%)	15 (34.9%)	6 (14%)

Among these patients were two brothers who had played with a brother and sister who were in the hospital with severe poliomyelitis. One little girl had an older sister in the hospital with severe paralysis, and another child had a visiting cousin who developed the disease two days after arrival at her home. One 3-year-old boy had weakness in one leg and a normal spinal tap. He was sent home only to return one week later with marked paralysis in the leg and again the spinal tap was normal. One young man was admitted with severe paralysis in both legs. He gave a history of having been admitted to another hospital with a tentative diagnosis of poliomyelitis but was sent home because the cytology was normal. Paralysis developed three days later.

During the epidemic period many patients were sent into the hospital with symptoms suggestive of poliomyelitis. In 1949, during July and August, 38 such cases were admitted and were variously diagnosed as meningitis, rheumatic fever, scurvy, influenza, encephalitis, and abortive poliomyelitis.

DISCUSSION

The finding of a normal spinal fluid in an indisputable case of poliomyelitis may be due to many factors. It is fairly well established that the cell count should be done as soon as possible after the fluid is drawn to be accurate. A lapse of even five minutes can make a difference. Most laboratories are a considerable distance from the bedside of the patient; frequently several spinal taps are done on different patients in succession, and the spinal fluids taken to the laboratory together. There is thus a delay which may be as long as half an hour. As a high percentage of cases have cell counts between 10 and 50 cells, the time factor can be significant. Another factor which influences the spinal fluid count is the day of disease when the spinal fluid is collected. During the past two years, and especially in 1949, an increasing number of patients have been admitted to the hospital within twenty-four hours after the onset of the disease. In Table IV may be seen the number of cases with normal cytology in relation to the day of disease when the spinal tap was done. Thirty-two per cent of the normal spinal fluids were from patients ill twenty-four hours or less, and 74.6 per cent in the first four days of illness.

Repeat spinal taps are of great importance. Of 22 patients with a normal spinal fluid, 61 per cent had abnormal findings on the second spinal tap. In some hospitals repeat taps are done daily for several days. In 1949 we were

TABLE IV. FORTY-THREE CASES WITH NORMAL SPINAL FLUIDS IN RELATION TO DAY OF DISEASE

DAY OF DISEASE	NO. OF CASES	PER CENT OF TOTAL
1	14	32.6
2	6	14.0
3	6	14.0
4	6	14.0
5	1	2.3
6	1	2.3
7	2	4.6
8	2	4.6
9	2	4.6
10	2	4.6
11	1	2.3

not able to do as many repeat taps as were carried out in other years because of the high incidence of admissions during July and August, and in that year we had the highest number of normal spinal fluids. Of the 43 cases with normal spinal fluids, 34 or 79 per cent had only one spinal tap done and the other 9 had only two. Repeat spinal taps often result in bizarre and unpredictable findings in the spinal fluids as illustrated in Table V.

TABLE V. RESULTS OBTAINED FROM REPEAT SPINAL TAPS

NAME	DAY OF DISEASE	CELL COUNT	PROTEIN MG.	TYPE OF CASE
M. L.	2	1	30	Slight paralysis
	4	30	130	
	7	3	80	
	37	1	50	
S. F.	4	6	25	Spinobulbar
	6	69	75	
	8	12	70	
	16	3	125	
A. B.	2	29	—	Moderate paralysis
	4	0	10	
	5	140	35	

There are also errors in the day of onset of the disease as given by parents or patients. Many times the date of onset is reported as the day when the weakness was first noticed and this may have been several days after the actual onset of the disease. A difference of three or four days can greatly influence the findings in the spinal fluid.

SUMMARY

1. From June, 1944, through December, 1949, there were admitted to the Geisinger Memorial Hospital 320 cases of acute anterior poliomyelitis. Forty-three or 13.8 per cent of the patients showed no abnormal findings in the spinal fluid although they had the characteristic signs and symptoms of the disease. Five of the patients were nonparalytic at the time of discharge while the other 38 patients showed slight to severe paralysis. At the end of a three months' follow-up, 51.1 per cent had completely recovered, 34.9 per cent had residual weakness, and 14 per cent had severe paralysis.

2. It was observed that 32.6 per cent of these patients had the spinal tap done on the first day of the disease and 74.6 per cent within the first four days.

3. The diagnostic criteria for paralytic and nonparalytic poliomyelitis as formulated by the National Conference on Recommended Practices is the best outline to follow in the diagnosis of this disease at the present time.

4. The diagnosis of acute poliomyelitis should be made from the clinical observations with the aid of the spinal fluid findings by a physician qualified by experience and training to make such a diagnosis.

REFERENCES

1. Van Rooyen, C. E., and Rhoades, A. J.: Virus Diseases of Man, New York, 1948, Thomas Nelson & Sons, p. 922.
2. Kolmer, J. A., Freese, A. E., Motsunami, T., and Meine, F.: Studies of the Cerebrospinal Fluid in Acute Anterior Poliomyelitis, Am. J. M. Sc. 154: 720, 1917.
3. Meals, R. W., and Bowers, A. G.: Poliomyelitis, J. Lab. & Clin. Med. 17: 409, 1932.
4. Conway, J. A., and Bigwood, D. E.: Observations Made During a Poliomyelitis Epidemic in 1944 in Hornell State Health District, New York, New York State J. Med. 46: 275, 1946.

BLEEDING DUODENAL ULCER IN INFANCY: A SURGICAL PROBLEM

Report of Two Cases Treated Successfully by Surgery

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BLEEDING duodenal ulcer in infants under 1 year of age deserves more than a passing reference in the differential diagnosis of hemorrhage from the gastrointestinal tract. As a rule, one usually thinks of a Meckel's diverticulum or a rectal polyp in an infant with bleeding from the gastrointestinal tract rather than a duodenal ulcer. The importance in making the diagnosis in an infant is considerably greater than in an adult with the same condition, for if left untreated surgically the infant practically always succumbs. In the adult, conservative treatment is the method of choice and unless the bleeding is massive, surgery is not performed after the first episode. In the infant under 1 year of age, conservative treatment has usually terminated in a fatality as attested by most reports in the literature.

It is probable that some infants with bleeding duodenal ulcer quiet down under conservative treatment, but the margin of safety is so small that the risk of delay seems to outweigh the danger of operation. With the advances in anesthesia, the better understanding of fluid balance, and the availability of chemotherapy, surgery of the infant is no longer considered a grave procedure.

In the past, the diagnosis of duodenal ulcer was usually made in adults, and it was not until Helmholz,[1] in 1909, reported nine cases of ulcer of the duodenum found at post mortem in atrophic infants that the occurrence of duodenal ulcer in infancy was considered of clinical significance. He suggested ischemia caused by arteriole spasm and infection as possible etiological factors. Prior to the appearance of Helmholz's article there had been sporadic case reports including one by Borland[2] in 1903, in an infant 8 months old, who, while under treatment for an acute eczema, developed hematemesis and died. Post-mortem findings revealed a duodenal ulcer. In 1913, Holt[3] summarized this condition reporting on ninety-one cases found in the literature and added four of his own. Of sixty-five patients in which the age was known, 70 per cent were between the ages of 6 weeks and 5 months. In addition, there were nine cases in the newborn infant and seven cases of infants over 5 months of age. His conclusion was that this condition primarily existed in the same age group in which marasmus occurred. There was no definite report of patients with bleeding duodenal ulcer but he emphasized that hemorrhage was a necessity to the diagnosis. More than one-third of the group had no symptoms during life referrable to the ulcer while in the other patients death usually occurred with

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collapse, hemorrhage, and perforation with peritonitis. In conclusion, he stated that surgical treatment for duodenal ulcer in this age group was as yet inadvisable in most cases. Theile,[4] in 1919, reported on thirty-one cases of children dead of melena in infancy and childhood from duodenal ulcer. Palmer,[5] in 1921, reporting on forty-five cases with an average age of 3½ months, emphasized again the marasmic appearance of these babies and stated that hematemesis and melena if present were usually terminal. Paterson,[6] in 1922, in an article on duodenal ulcer in infancy, mentioned a case report of T.D. Lister in 1899, of melena neonatorum in a child 3 days old. At autopsy, the child had a well-defined duodenal ulcer. Brockington and Lightwood,[7] in 1932, cited a case at post mortem where the ulcer had penetrated all coats and on slight manipulation duodenal fluid passed through the ulcer bed. This finding was similar to that found at operation in Case 1 as will be mentioned more in detail later. It was not until 1941, following the article by Bird, Lemper, and Mayer,[8] that bleeding duodenal ulcer in infants received proper attention. They stressed the fact that in infants the diagnosis of duodenal ulcer was rarely made unless the complications of hemorrhage or perforation developed. Obstruction, another complication of duodenal ulcer in adults, was rarely if ever seen. Much speculation as to the etiology of duodenal ulcer in infants is scattered throughout the literature. The most common theory advanced is that of acute infection not necessarily of the gastrointestinal tract as was noted in Case 2 of this report. The general inference from a review of the literature is that the condition is most likely to be found in emaciated or marasmic infants. It is interesting that in both of these infants this was not true; in fact, in one instance the infant appeared very well nourished. Burns and scalds and trauma by other agents may conceivably be factors. It would be difficult to explain this condition in infants on the basis of a psychiatric disturbance. In 1911, Wilkie,[9] commenting on the blood supply of the duodenum, mentioned the possibility of a supraduodenal artery supplying the upper two-thirds of the anterior surface and the upper one-third of the posterior surface of the first part of the duodenum. It usually stems from the gastroduodenal or hepatic artery and might well be the vessel responsible for the sudden severe hemorrhage that occurs.

The two cases summarized below were females in whom bleeding was the only clue to the probable diagnosis. Exploratory laparotomy was considered mandatory as soon as the infants could be put in the best possible condition for surgery.

CASE REPORTS

CASE 1.—P. L. C., a white female aged 1 year, was admitted Dec. 25, 1949.

Past History.—She was born by cesarean section because of cephalopelvic disproportion. She was formula fed without supplementary vitamin D. She took ascorbic acid because of allergy to orange juice.

Present Illness.—She had been healthy until the present illness. Six days prior to admission she developed vomiting and diarrhea which persisted for four days and ran a course typical of an outbreak of gastroenteritis which at the time affected children of all ages in Rochester. Two days prior to admission she received one injection of penicillin and resumed oral feedings. Although parents noted that she passed one tarry black stool the day before, there was no

further incident until the afternoon of the day of admission when convulsions suddenly appeared. She was brought immediately to the emergency room of the Genesee Hospital.

Physical Examination.—The temperature was 101° F. The pulse exceeded 160. Respirations were very irregular and impossible to count. The patient was a well-developed, well-nourished, comatose white female infant having clonic movements of extremities and facial muscles. She was extremely pale and quite obviously in shock although cyanosis was not present. Respirations were very irregular and shallow. No breath sounds could be heard. Heart action was rapid and regular. No localizing signs were found. During examination the patient passed large amounts of tarry black stool.

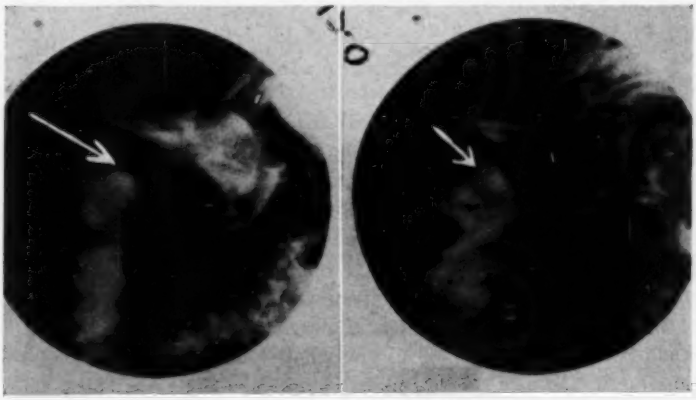

Fig. 1.—Postoperative films showing normal emptying of duodenal cap.

Hospital Course.—One attempt at controlling the convulsions was made using 1 gr. phenobarbital sodium intramuscularly. At this point, respirations ceased entirely, and the patient was maintained with artificial respiration and oxygen. Because of the baby's precarious condition and the rather obvious state of exsanguination into the gastrointestinal tract, no laboratory data were obtained. A transfusion of 500 c.c. of whole blood was given through a scalp vein while a cut-down was performed on an ankle vein. Following the transfusions, the patient's condition improved markedly. Her color became normal, and good respirations were established. A short time later the patient again started to have convulsions. A lumbar puncture at that time revealed normal cerebrospinal fluid. The convulsions were controlled with 1 c.c. paraldehyde intramuscularly. A blood count done about seven hours after the transfusions showed a hemoglobin of 9 Gm. and red blood count of 3.18 million. Patient continued to pass tarry stools for the next two days. She was maintained on continuous intravenous fluids and small blood transfusions. On the third hospital day, an exploratory laparotomy was performed. The opinion of the pediatric and surgical observers was that a bleeding lesion, possibly in a Meckel's diverticulum, would be found below Treitz ligament. An upper gastrointestinal tract lesion was not expected because of the absence of hematemesis. At operation, no lesion of any type was disclosed despite thorough examination of the entire small and large intestinal tract, although the distal two-thirds of the small bowel was found to contain blood. The patient was returned to the division in good condition. During the next five days she continued to pass

tarry stools and clots of blood. She was maintained throughout this time with small transfusions. On the sixth postoperative day, a surgical exploration was performed by one of the authors (S.J.S.). A small ulcer covered with only thin membrane was found just distal to the pylorus on the lateral anterior wall of the duodenum. The ulcer was opened and a large clot removed with subsequent profuse hemorrhage. The artery feeding the ulcer appeared to be a large-sized branch of the gastroduodenal or possibly the supraduodenal artery. The bleeding was controlled and the incision was extended down the duodenum and up across the pylorus and stomach, and an anastomosis in the opposite direction was made. The patient returned to the division in good condition and the postoperative course was uneventful. The patient had no more melena and was discharged on Jan. 16, 1950, twenty-two days after admission. She was seen again on March 10, 1950, and an upper gastrointestinal series was done. No lesion or obstruction was demonstrable by x-ray (Fig. 1). The patient appeared well and presented no evidence of any disturbance of the gastrointestinal tract.

Case Discussion.—There are several features about this infant that merit comment. Cerebral anoxia caused by the profound acute anemia and the concomitant shock undoubtedly was responsible for the convulsions. The experimental conclusions of Rossen, Kabat, and Anderson[10] on the occlusion of cerebral blood supply was well borne out in this instance, in that convulsions and coma occurred immediately after the anoxia had been produced. The history of gastroenteritis preceding the gastrointestinal tract bleeding suggests the possibility of this being the exciting cause in the development of the ulcer. The replacement of blood loss with 500 c.c. of whole blood in an infant of 1 year of age might at first glance appear to be excessive. However, there were no ill effects, and following this transfusion no attempt was made to maintain the hemoglobin above 10 Gm. Lumbar puncture was performed following the transfusion because of the recurrence of convulsions which made it necessary to exclude the possibility of a central nervous system lesion. There are a few points worthy of mention relative to the surgical approach. At the first operation, the surgeon, suspecting a Meckel's diverticulum, did not carry his incision high enough to allow thorough exploration of the first portion of the duodenum. This is well to remember in exploring infants suspected of having pathological conditions in the right upper abdomen. When the infant was explored the second time it was not until the previous incision had been extended upward several inches that a satisfactory view of the duodenum could be obtained. Ladd and Gross,[11] commenting on the surgical treatment of perforation which this infant actually presented at operation, state that *surgical closure* of the hole is all that is required and feel that plication or excision of the ulcer should never be done because of the contraction that might follow. In this instance, it was decided that a pyloroplasty should be performed, and the follow-up x-rays taken three months after surgery revealed a relatively normal opening.

Case 2.—J. S. (S.M.H. No. 265042), a 10-month-old baby girl, was admitted to Strong Memorial Hospital on Aug. 30, 1947, because of high fever. The patient had been perfectly well until twenty-four hours before admission, when she became irritable and developed fever and malaise. The following day the

fever persisted and the child seemed quite acutely ill. There had been no known recent exposure to contagious disease, and there had been no nausea, vomiting, or diarrhea. The past history revealed that the child had had a normal birth, and had normal development and feeding habits up until the time of admission.

Examination revealed the temperature to be 40° C., pulse 155, respirations 70. There was no cyanosis or evident dyspnea. The patient was a well-developed, well-nourished white female infant appearing very irritable and acutely ill. Examination revealed reddening of the left eardrum and injection of the tonsils and posterior pharynx. The remainder of the physical examination was essentially negative. Laboratory findings on admission were: red blood count 4.43 million; hemoglobin 13.5 Gm. per cent; white blood count 14,800, differential showed 60 per cent polymorphonuclear, leucocytes; urine negative. The clinical impression at the time of admission was catarrhal otitis media, right and acute nasopharyngitis. The patient was given sulfadiazine, and fluids were forced. On the second hospital day, the child was eating very poorly and continued to have an elevated temperature. On that day, she received 400 c.c. of 2½ per cent dextrose solution intravenously. On the third day after admission, the child had a sudden onset of rather massive emesis, characterized by dark brown coffee-ground material. Shortly after this, the child passed a tarry stool, and shortly following this, a grossly bloody stool. Red blood count at that time was 2.34 million and hemoglobin was 7.2 Gm. per cent. The patient became very pale and showed signs of shock. She was given 140 c.c. of whole blood intravenously. At this time the blood clotting time, bleeding time, and prothrombin time were all within normal limits. Examination after the transfusion revealed increased resistance in the right upper quadrant of the abdomen and questionable tenderness in this area. Because of the hematemesis, it was thought that the hemorrhage probably originated either with a gastric or duodenal ulcer or from esophageal varices. The baby continued to have grossly bloody stools and required repeated blood transfusions to maintain the red blood count and the hemoglobin. On the third day following the first evidence of hemorrhage, laparotomy was decided upon because of continued bleeding.

Exploration was performed by Dr. Earle B. Mahoney under ether anesthesia through a right rectus longitudinal incision. On opening the abdomen, a small amount of clear, colorless fluid was encountered. The stomach and first portion of the duodenum were first explored and no abnormality was noted. At the time of exploration there was no gross evidence of blood in the stomach. The small bowel was then carefully examined and no evidence of a Meckel's diverticulum was found, and there was no evidence of a lesion in the large bowel. The duodenum was then re-explored by mobilizing the second and third portions and a small ulcer was found on the anterior surface of the duodenum. The ulcer was on the verge of rupture and only a thin, grayish membrane of serosa covered the ulcerated area. The ulcer lay anterior to the point where the common duct entered the duodenum so it was excised, using elliptical longitudinal incisions, removing a small margin of normal duodenum. The opening in the duodenum was then closed transversely using two layers of 00000 silk on an atraumatic needle. The abdominal wound was closed with interrupted fine silk throughout. The patient withstood the operation well and received supportive transfusions. The postoperative convalescence was uneventful except for the passage of a tarry stool on the ninth postoperative day. The patient was discharged on the fifteenth postoperative day at which time the wound was well healed and the child appeared to be in good condition. The red blood count at the time of discharge was 5 million, hemoglobin 15 Gm. The patient was readmitted to the hospital recently on March 3, 1950, with otitis media. History taken at that time revealed no symptoms referrable to the ulcer or obstruction since discharge in 1947. She had been well and development was normal.

Case Discussion.—It is interesting that in this infant a history of upper respiratory infection in an otherwise normal child preceded the onset of hematemesis and melena. The presence of hematemesis suggested that the bleeding was proximal to the ligament of Treitz. The surgery performed was not unlike that in the first case.

SUMMARY

1. Two cases in female infants under 1 year of age are reported successfully treated by surgery during acute hemorrhage.

2. Bleeding duodenal ulcer should always be seriously considered in the differential diagnosis of gastrointestinal hemorrhage in infancy.

3. Hematemesis is not a necessary criterion to establish the diagnosis.

4. The margin of safety in conservative treatment of this condition of the infant is considerably reduced in contrast to that of the adult.

5. The advances in preoperative and postoperative care combined with modern surgical technique remove this condition from the hopeless field of therapy.

REFERENCES

1. Helmholz, Henry F.: The Relation of Duodenal Ulcers to Atrophic Conditions of Infants, Arch. Pediat. **26**: 661, 1909.
2. Borland, Hugh Howie: .Infantile Acute Eczema; Haematemesis; Duodenal Ulcer; Death, Lancet **2**: 1084, 1903.
3. Holt, L. Emmett: Duodenal Ulcer in Infancy, Am. J. Dis. Child **6**: 381, 1913.
4. Theile, P.: Ergebn. d. inn. Med. u. Kinderh. **16**: 302, 1919.
5. Palmer, Dudley White: Duodenal Ulcer in Infancy, Ann. Surg. **73**: 545, 1921.
6. Paterson, Donald: Duodenal Ulcer in Infancy, Lancet **1**: 63, 1922.
7. Brockington, C. F., and Lightwood, R.: Duodenal Ulceration in Infants, Lancet **2**: 1209, 1932.
8. Bird, Clarence E., Lemper, Margaret A., and Mayer, Jacob M.: Surgery in Peptic Ulceration of Stomach and Duodenum in Infants and Children, Ann. Surg. **114**: 526, 1941.
9. Wilkie, D. P. D.: The Blood Supply of the Duodenum With Special Reference to the Supra-duodenal Artery, Surg., Gynec., & Obst. **13**: 399, 1911.
10. Rossen, R., Kabat, H., and Anderson, J. P.: Acute Arrest of Cerebral Circulation in Man, Arch. Neurol. & Psychiat. **50**: 510, 1943.
11. Ladd, William E., and Gross, Robert E.: Abdominal Surgery of Infancy and Childhood.

Case Reports

PERFORATED GASTRIC ULCER IN A NEWBORN INFANT

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PEPTIC ulceration is a well-authenticated though rare disease of infancy and childhood, occurring at all ages from the first day onward. The condition was recognized over 100 years ago when Cruveilhier[1] described the presence of multiple gastric ulcers in three infants at the respective ages of 1, 2, and 4 weeks.

In 1941, Bird, Limper, and Mayer[2] reviewed all cases of peptic ulcers in children that were recorded in the literature and noted that of 243 reported cases, thirty-eight occurred between birth and 14 days of age, and that of these only twelve were gastric ulcers. In the age group of 15 days to 1 year, forty-three duodenal ulcers were reported as compared with eight gastric ulcers. Rosenberg and Heath,[3] in 1946, reported a case of acute gastric ulcer with perforation in the second month of life in one of premature twins. In view of the comparative rarity of this condition, the following case of gastric ulcer with perforation in a newborn infant is being presented.

CASE REPORT

Male child R. I. was born on July 30, 1949. The duration of labor was four hours. The child breathed and cried spontaneously. The delivery was normal and spontaneous. No abnormal physical findings were noted, and the infant was transferred to the nursery in apparently good physical condition. The mother was 34 years old, gravida iv para iii. She was a pre-eclamptic who received antisyphilitic therapy consisting of 6,000,000 units of penicillin followed by weekly injections of bismuth and Mapharsen. Treatment was initiated in the sixth month of pregnancy.

On the morning of July 31, the day after delivery, it was noted that the infant was cyanotic and that he took the formula poorly. Examination revealed a well-developed Negro male child. He weighed 2.8 kg. and measured 51 cm. Respirations were shallow. Breath sounds were present throughout both lung fields. The abdomen was soft and nontender. Stools were normal, and the patient had not vomited.

The following day, August 1, the patient continued to be cyanotic when not receiving oxygen. Respirations ranged between 30 and 36 per minute. No chest retractions nor impairment of breath sounds were noted. The infant was placed on penicillin prophylactically.

On August 2 and 3, the baby was still cyanotic, and tachypneic. The chest, heart, and abdominal examinations were negative. On August 4, the fifth day after delivery, the temperature was 38.8° C., and the general condition of the patient was poor. The abdomen was markedly distended, firm, and tympanitic.

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Rectal examination revealed no abnormalities. Levine and rectal tubes were passed and left in place. Hydration was maintained with fluids given parenterally. There was no vomiting. Stools were small and green.

Laboratory Data.—The red blood cell count was 4,810,000 and the hemoglobin was 12.8 Gm. A flat and upright x-ray of the abdomen on August 4, taken prior to the passage of the Levine tube, revealed a "massive pneumoperitoneum with high position of the diaphragm and displacement of the abdominal viscera" (Fig. 1).

The infant expired before operation could be performed.

Fig. 1.—Roentgenogram showing pneumoperitoneum.

Autopsy Findings.—At necropsy a longitudinal incision of the abdominal wall was made. The peritoneum was opened under water, and gas bubbles escaped. The abdominal cavity revealed the presence of 150 c.c. of brown turbid fluid containing particles of thick material some of which were adherent to the viscera. Loops of small intestine were densely matted together. The diaphragm was high and palpable at the level of the third intercostal space bilaterally. The liver and stomach presented a relative ptosis. The stomach revealed an injected, finely granular serosal surface. The mucosa was hemorrhagic. On the serosal surface of the lesser curvature of the pyloric region of the stomach, a fibrinopurulent exudate covered an underlying perforation which measured 2 mm. in diameter. Its jagged wall pouted into the abdominal cavity. The mucosa adjacent to the perforation had punctate hemorrhages. The spleen, liver, pancreas, kidneys, and adrenals were normal. The lungs were atelectatic. The heart presented no abnormalities.

On section, the serosal surface of the stomach was covered with a thick, recent fibrinopurulent exudate and in this same area there was discontinuity of the mucosa, submucosa, and muscularis. This discontinuity formed an ulceration with a base consisting of fibrinopurulent exudate and degenerating mural elements. The mucosa bordering the ulcer showed evidence of autolytic changes. The submucosa, in addition, revealed the presence of dilated blood vessels and an infiltration of lymphocytes, polymorphonuclear leucocytes, and plasma cells (Fig. 2).

Smear of the abdominal fluid revealed gram-negative organisms. *Aerobacter aerogenes,* paracolon bacilli, and gamma streptococci were found on culture.

Fig. 2.—Photomicrograph showing ulceration of the stomach wall.

COMMENT

The majority of infantile peptic ulcers occur in the early weeks of life with a preponderance of duodenal ulcers over gastric ulcers. It is not generally conceded that peptic ulcers originate in utero. In Guthrie's[4] review of the literature it was noted that Theile and Ballantine consider them to arise almost invariably after birth, and that Ladd and Gross have described them in stillborn infants.

Hemorrhage from the stomach or bowel is generally considered to be the most important sign during the newborn period. After the neonatal period peptic ulceration is most frequently associated with marasmus. Hypertrophic pyloric stenosis may be simulated if the peptic ulcer causes spasm of the pylorus. These findings were not present in this instance.

Certain circumstances incidental to birth and early infancy are proposed by Guthrie[4] to explain the occurrence of peptic ulcer at this early age. She believes that circulatory instability, especially in prolonged labor, tends to devitalize the duodenal mucosa. Any damaged area, therefore, is liable to digestion by the gastric juice which, according to Miller[5] has remarkably high

acidity in the first forty-eight hours of life. Direct trauma to the gastric mucosa may occur accidentally during resuscitation at birth. Further congestion and possibly hemorrhage may result from hyperperistalsis associated with congenital pyloric stenosis.

Mucosal irritation may be produced by drugs or unsuitable feedings. There was no evidence in the case presented to suggest that these were responsible. The only factors that could be considered in this instance as possible etiological agents are:

1. Syphilis.
2. Antisyphilitic treatment.
3. Pre-eclampsia.

However, considering the frequency of this combination and the rarity of ulcers in the newborn infant, it is questionable if they were the direct causes.

SUMMARY

A case of a perforated gastric ulcer in a newborn infant delivered of a pre-eclamptic syphilitic patient has been presented. It is unusual in that typical symptoms were not present.

We are indebted to Solomon Weintraub, M.D., Director of Pathology, for autopsy material and valuable histological sections.

REFERENCES

1. Cruveilhier, J.: Anatomie Pathologique du Corps Humain, 1829-1835, p. 15.
2. Bird, C. E., Limper, M. A., and Mayer, J. M.: Ann. Surg. 114: 526, 1941.
3. Rosenberg, A. A., and Heath, M. H.: J. PEDIAT. 26: 93, 1946.
4. Guthrie, Katherine J.: Arch. Dis. Childhood 17: 82, 1942.
5. Miller, R. A.: Arch. Dis. Childhood 16: 22, 1941.

PNEUMOCOCCAL MENINGITIS WITH HYPERGLYCEMIA AND DEVELOPMENT OF SUBDURAL EFFUSION; SUCCESSFUL TREATMENT WITH CHLORAMPHENICOL

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CHLORAMPHENICOL has been shown to be an effective therapeutic agent against bacterial and some rickettsial and viral diseases. Successful treatment of pneumonia caused by the pneumococcus has been reported,[1, 2] but a search of the literature fails to reveal any reported cases of pneumococcal meningitis treated with Chloromycetin.*

An unusual case of pneumococcal meningitis complicated by hyperglycemia and the development of subdural effusion, with successful treatment with chloramphenicol, is reported in detail.

CASE REPORT

J. T. was a 4-month old Negro male infant who was admitted to the Babies and Children's Hospital of Cleveland on April 17, 1950, because of a generalized convulsion. He had apparently been well until forty-eight hours prior to admission. At this time his mother noted that he was less playful than usual, but he had no fever and took feedings well. Eight hours later the mother felt that he had fever and breathing was rapid. On the day before admission, fever persisted but the infant continued to play with toys over the bed and fed well. Early on the night before admission he was seen in the Emergency Room with a temperature of 39° C. and a left suppurative otitis media. The fontanel was flat; the infant was alert and playful. The purulent exudate was gently cleansed with a sterile applicator by the pediatric resident; he was given procaine penicillin 300,000 units intramuscularly, and advised to have aspirin, grain ¼ every four hours as needed for fever, and instructed to return to the Out-Patient Department the following afternoon. After returning home, the infant was noted to arch his back, the cry became high-pitched, and he became more lethargic with intermittent bouts of hyperirritability. There was no abatement of the fever. On the morning of admission, the mother noted that he was somewhat unresponsive and a short time before admission he had a generalized convulsion, both tonic and clonic in nature, associated with ocular asynergy and excessive salivation. The patient was brought immediately to the Admitting Ward of Babies and Children's Hospital where he was given Sodium Amytal, grain ½, intravenously, which terminated the convulsion, and he was admitted to the ward.

Past history revealed that the patient was of healthy parents, born at term by elective cesarean section. The birth weight was 6 pounds, 15 ounces, and the infant breathed and cried immediately. He had been breast fed with added cereals and vegetables and adequate vitamin supplements. He had gained weight well and had always been a good eater. Motor and mental development

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had been entirely normal. He had had frequent upper respiratory infections without associated fever, but there was no history of previous convulsions, otitis media, or exposure to acute infectious disease.

Family history was noncontributory. There was no history of diabetes on either side of the family.

Examination on admission revealed a well-developed and well-nourished 4-month old Negro male infant, who appeared acutely and seriously ill, and who was unresponsive, due to the previous sedation. Temperature was 39° C., pulse 180, respirations 64, and blood pressure 90/58. The head measured 42 cm., chest 38 cm. The skin was hot and moist without petechiae. There was no glandular enlargement. The head was mesocephalic; the anterior fontanel admitted two fingers, was tense and bulging one-half inch above the level of the scalp. Extraocular movements were purposeless; the pupils were constricted, regular, round, and equal. The fundi after a mydriatic were normal. The left auditory canal was filled with a yellow purulent exudate obscuring the drum, and the right tympanic membrane was injected. The nose was filled with a thick exudate. The buccal mucosa was pale and the pharynx was moderately injected with excessive postnasal mucus. There was questionable rigidity of the neck in the anteroposterior axis; the trachea was in the midline. The percussion note was impaired over the right lower lung field posteriorly with suppression of breath sounds over this area with inconstant rhonchi over the left upper lobe. There were no cardiac enlargement or murmurs. The rate was very rapid. The abdomen was relaxed and soft without palpable masses or viscera. Kernig and Brudzinski reflexes were absent, and deep-tendon reflexes were hypoactive.

Immediately after admission a lumbar puncture was performed, and cloudy cerebrospinal fluid was obtained under increased pressure. This contained 1,550 white blood cells per cubic millimeter, with 95 per cent segmented neutrophiles. A gram-positive diplococcus, compatible with pneumococcus, was demonstrated on direct smear. Spinal fluid was sent to the laboratory for protein, sugar, and chloride measurements; blood was drawn for culture and sugar determination. Hemoglobin on entry was 8.26 Gm.; red blood cells were 4,470,000 per cubic millimeter; white blood cells were 20,650 per cubic millimeter with 27 per cent unsegmented polymorphonuclear leucocytes and 38 per cent segmented polymorphonuclear leucocytes. Urinalysis obtained shortly after entry revealed a four-plus sugar and three-plus acetone with an occasional white blood cell and no albuminuria. Chemical determinations on the spinal fluid were reported shortly after admission and the sugar was 81 mg. per 100 c.c. Blood sugar drawn at the same time was 180 mg. per 100 c.c. The values preceded any parenteral fluid treatment. On requestioning the mother, it was found that the patient had refused all feedings except water for twelve hours before admission. Chest roentgenogram showed bilateral infiltration, most prominent at the right base.

Since a good response followed treatment of a patient with severe bronchopneumonia and pneumococcal septicemia with chloramphenicol in this hospital, it was decided to treat the reported patient with this drug. He was started on massive doses of Chloromycetin, 750 mg. as an initial dose and 350 mg. per kilogram of body weight per day in divided doses, every three hours, by mouth. On the morning after admission, nose and throat cultures were reported as showing predominantly pneumococcus; both spinal fluid and blood cultures were positive for pneumococcus, type 14. In vitro studies of this organism revealed that it was sensitive to less than three gamma per cubic centimeter of chloramphenicol. Fasting blood sugar on the morning after admission was 200 mg. per cent. All fractional urine specimens up to this time had shown three- to four-plus glycosuria (which was identified as glucose), and two- to three-plus acetone. The patient had taken fluids well by mouth, not requiring parenteral fluids. He was

on an evaporated milk (one part) and water (two parts) formula, with 5 per cent Karo added. It could not be determined at this time whether the patient represented a true diabetic or whether hyperglycemia and glycosuria only represented a hyperglycemic response to central nervous system infection. It was decided to manage the patient as a diabetic, covering the hyperglycemia with small doses of insulin. He was first given regular insulin, 3 units.

Lumbar puncture, as well as blood culture, was repeated twenty-six hours after admission. Only 1.5 c.c. of spinal fluid could be obtained via the lumbar route; the fluid was slightly cloudy, and contained 351 cells, 84 per cent of which were polymorphonuclear leucocytes. Smear and culture were both negative for pneumococcus. Spinal fluid sugar was 116 mg. per cent. Blood culture taken on this date was subsequently reported negative. Thus after twenty-six hours of treatment with Chloromycetin, both the spinal fluid and the blood were sterile. The white blood count was still 19,000 per cubic millimeter. Temperature remained 39.5° C., rectally. The anterior fontanel was tense and bulging even after the lumbar puncture. Carbon dioxide combining power, pH, nonprotein nitrogen, serum chloride, sodium, potassium, calcium, and phosphorus were all within normal limits.

It was decided to continue chemotherapy as described, to obtain fractional urine specimens when possible, although this was quite difficult because of patient's age, and to obtain frequent blood sugars and treat the patient with insulin accordingly. (See Charts I and II for data.) On the night of the second hospital day, the patient had one episode of generalized twitching which was controlled by sodium phenobarbital. Blood sugar at this time was 92 mg. per 100 c.c. Ventricular taps were contemplated to relieve the increased intracranial pressure, but following lumbar puncture, during which fluid and dynamics were still sluggish, the fontanel tension was decreased. Beginning the second hospital day, the patient began taking fluids poorly by mouth. Parenteral fluid treatment proved quite a problem as it was felt unwise to give the patient excessive dextrose because of the coexisting hyperglycemia or, conversely, excessive amounts of fluid containing sodium chloride which would tend to increase cerebral edema and with it the intracranial pressure. As a result, the patient was given minimal daily requirements of Ringer's solution intravenously and by hypodermoclysis, and also small amounts of distilled water subcutaneously and by proctoclysis very slowly. Frequent observations revealed no evidence of subcutaneous irritation or slough.

By the afternoon of the third hospital day, the temperature had dropped to 38.5° C., and there was slight general improvement with lessening of lethargy, and with no recurrence of the muscular twitchings. By the morning of the fourth hospital day, there was very definite improvement. The patient was more alert, the temperature had dropped to 37.8° C., and the patient began taking feedings better by mouth. On small doses of insulin the hyperglycemia and glycosuria were fairly well controlled. Lumbar puncture repeated at this time showed much freer flow of spinal fluid which was clear, with free dynamics, and contained 5 white blood cells, protein 35 mg. per cent, sugar 77 mg. per cent. Smear and culture were again negative. Repeat blood culture at this time was negative. The patient had been given several small transfusions which corrected his anemia. Other than a temperature spike to 38° C. on the fourth hospital day, the temperature remained normal. From that time on the patient continued to improve, became alert, playful, smiled, and played with toys over bed. He took all feedings well and began to gain weight.

On the sixth hospital day, Chloromycetin was reduced to 50 mg. per kilogram body weight. Frequent nonprotein nitrogen determinations were obtained, all of which were normal. On this day it was noted for the first time that the

CHART I

DATE	TIME OF COLLECTION	URINE SUGAR	ACETONE	$FECl_3$	BLOOD SUGAR	CSF SUGAR	REGULAR INSULIN
4/17/50	3:00 P.M.	4+	3+		180	81	
	10:00 P.M.	4+	3+	1+	192		
4/18/50	3:00 A.M.	4+	3+	1+	400		
	8:00 A.M.	4+	2+	1+	200		3 units
	1:00 P.M.	2+	1+	1+	180	116	
	8:30 P.M.						3 units
	10:00 P.M.	1+	1+	0	92		
4/19/50	3:00 A.M.	1+	TR	0			
	8:00 A.M.				111		
	1:30 P.M.	0	0	0	395		
	5:30 P.M.	TR	0	0			3 units
	10:00 P.M.				120		
4/20/50	3:00 A.M.	2+	neg.	0	164		2 units
	8:00 A.M.				67		3 units
	10:30 A.M.					46	
	2:00 P.M.	0	0	0			
	4:30 P.M.				95		3 units
	10:00 P.M.				106		
4/21/50	1:00 A.M.	0	0	0	146		
	8:00 A.M.	0	0	0	112		
	11:00 A.M.	0	0	0			
	3:30 P.M.	0	0	0			3 units
	5:30 P.M.	1+	0	0			
	12:00 M.				103		
4/22/50	1:00 A.M.	0	0				
	8:00 A.M.				110		
	9:30 A.M.	1+	0	0			
	10:30 A.M.						3 units
	10:00 P.M.				212		
4/23/50	1:00 A.M.	1+	0	0			2 units
	8:00 A.M.				150		3 units
	9:30 A.M.	TR	0	0			
	4:00 P.M.	0	0	0	112		
	11:00 P.M.				110		3 units
4/24/50	1:00 A.M.	TR	0	0			
	8:00 A.M.	0	0	0	87	77	
	3:30 P.M.				112		
	5:00 P.M.	0	0	0			
	10:00 P.M.				90		
4/25/50	8:00 A.M.	0	0	0	105		
	9:30 A.M.	0	0	0			
	3:30 P.M.				134		
	10:00 P.M.				108		
4/26/50	1:30 A.M.	0	0	0			
	3:00 A.M.				102		
	9:30 A.M.	0	0	0			
	3:30 P.M.				132		
	10:00 P.M.	0	0	0			
4/27/50	1:00 A.M.	0	0				
	8:00 A.M.	0	0	0	110		
	2:00 P.M.	0	0	0			
	10:00 P.M.	0	0	0			
4/28/50		0	0				
4/29/50		0	0		108		

CHART 1—CONT'D

DATE	TIME OF COLLECTION	URINE SUGAR	ACETONE	$FeCl_3$	BLOOD SUGAR	CSF SUGAR	REGULAR INSULIN
4/30/50		0	0				
5/ 1/50		0	0				
5/ 2/50		0	0				
5/ 3/50		0	0			71	
5/ 4/50		0	0				
5/ 5/50		0	0		92		
5/ 6/50		0	0				
5/ 7/50		0	0				
5/ 8/50		0	0				
5/ 9/50		0	0				
5/10/50		0	0				
5/11/50		0	0				
5/12/50		0	0		111		
5/13/50		0	0				
5/14/50		0	0				
5/15/50		0	0				
5/16/50		0	0				
5/17/50		0	0		109		
5/18/50		0	0				
5/19/50		0	0				
5/20/50		0	0				
5/21/50		0	0				
5/22/50		0	0				

GLUCOSE TOLERANCE

Date		4/28/50	5/9/50
Time:	F	108	98
	½ hr.	158	160
	1 hr.	166	155
	2 hr.	131	134
	3 hr.	124	118
	4 hr.	86	91

patient's hearing seemed impaired. This grew progressively worse so that he seemed totally deaf by the tenth hospital day. In the light of the recent work by Ingraham and his collaborators[5] and Smith,[6] concerning the high incidence of subdural collection of fluid in convalescent meningidides due to *Hemophilis influenzae* and pneumococcus who were not doing well, it was decided to do subdural taps. Bilateral subdural taps through the anterior fontanel were performed and 12 c.c. of markedly xanthochromic fluid, with a total protein of 1328 mg. per cent, were removed from the left subdural space, under increased pressure. Culture of this fluid was sterile. Only 1 c.c. of fluid was

obtained from the right subdural space. The following day, it was noted that on lowering the side of the crib, while the patient was asleep, he awoke and seemed to hear loud noises. Repeated subdural taps at regular intervals yielded decreasing amounts of sterile xanthochromic fluid with an elevated protein content. This was followed by a gradual improvement in the patient's hearing. Bilateral craniotomies were performed and a subdural membrane on the left was removed. Since operation the patient's hearing is apparently normal. Daily urinalyses showed no evidence of renal irritation. Beginning on the eighth hospital day, insulin was discontinued and blood sugars remained normal as well as the urinalyses remaining negative for sugar, acetone, and diacetic acid. The glucose tolerance tests were normal. Several checks of postprandial sugars were normal. Chloromycetin was discontinued on the twenty-second hospital day without temperature elevation or other untoward effects. Electroencephalograms at regular intervals showed a gradually diminishing dysrhythmia until a normal pattern was reached.

There was no increase in head size throughout the course of the illness.

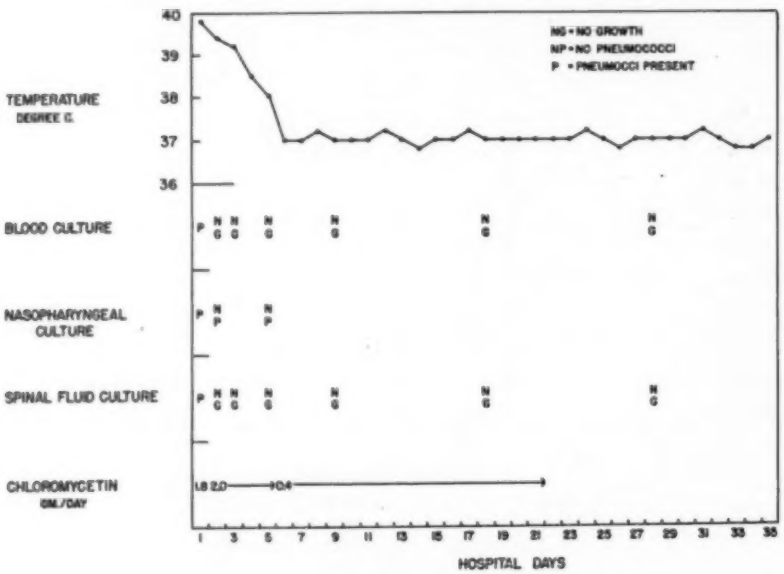

CHART II.

DISCUSSION

Chloramphenicol has been demonstrated to have a wide effective spectrum against disease entities caused by bacterial, viral, and rickettsial agents. The pneumococcus has been found to be quite susceptive in vitro to Chloromycetin, usually below 5 gamma per cubic centimeter.[1] Recinos, Ross, Olshaker, and Tribble[2] reported eighteen cases of pneumococcal pneumonia in children treated with chloramphenicol. They considered thirteen to have good response and five fair response. In their two cited cases, the blood cultures were sterile before institution of therapy. Hewitt and Williams[1] reported five cases of pneumococcal pneumonia in adults treated with chloramphenicol alone. All five patients had sterile blood cultures and all obtained a rapid response. In both the above

series, the nasopharynx became free of pneumococci within forty-eight hours after treatment with Chloromycetin was begun.

A search of the literature failed to reveal any reported cases of pneumococcal meningitis treated with chloramphenicol. We were prompted to try chloramphenicol in this case because of the reported experiences with this drug in pneumococcal pneumonia and favorable results in an 18-month old patient at this hospital with pneumococcal pneumonia and pneumococcal bacteremia treated with Chloromycetin. In the reported patient, blood and nasopharyngeal cultures revealed that the pneumococcus had disappeared in twenty hours after treatment was started, but the patient did not become completely afebrile for 120 hours.

Another interesting feature of this case was the hyperglycemia and glycosuria present at the height of the infection, but which disappeared when the infection became controlled. That glucose levels in the blood are controlled and affected by nervous influences has been known for years. Claude Bernard demonstrated that puncture of the floor of the fourth ventricle resulted in glycosuria, polyuria, and hyperglycemia. These centers for regulation of carbohydrate metabolism probably are located in the tuber cinereum of the hypothalamus (Leschke, Gnering, Hogler). The hyperglycemia produced by large doses of amidopyrine may be inhibited by the administration of brain stem narcotics, such as phenobarbital and barbital.[3] It is well known that hyperglycemia and/or glycosuria occur in various central nervous system infections, encephalidides, and also in cases of craniocerebral trauma. In a series of 336 cases of cerebral hemorrhage and trauma, reported by Merritt and Fremont-Smith,[4] 23 per cent had a spinal fluid sugar above 80 mg. per 100 c.c. These same workers in a study of spinal fluid in 966 patients with acute purulent meningitis demonstrated spinal fluid sugar greater than 80 mg. per 100 c.c. in only sixteen cases. In fifteen patients with blood sugars ranging between 150 and 200 mg. per cent, the spinal fluid sugar taken at the same time of the blood sugar ranged between 73 to 112 mg. per 100 c.c. with an average of 93 mg. per 100 c.c. A high serum sugar content may mask glycolysis and a decreased spinal fluid sugar in meningitis. Studies of chloramphenicol in dogs reveal no evidence of hyperglycemia or glycosuria attributable to the drug even though it was administered in large doses.

It seems unlikely that this patient had diabetes mellitus. The fact that his hyperglycemia disappeared after the central nervous system infection had cleared, and there was no history of diabetes in the family, and the parents' urinalyses were normal is against diabetes. In view of the evidence that central nervous system centers affect carbohydrate metabolism and serum sugar levels, it is logical to conclude that this patient's hyperglycemia was due to central nervous system infection. However, he is to be followed at long intervals as a potential diabetic. However, frank and permanent diabetes has never been produced by injury to the brain stem, according to Kuntz.[3]

The correction of deafness and other sequelae of purulent meningitis by proper management of subdural effusion (or possibly encysted spinal fluid in the subarachnoid space) is certainly an important concept. No final conclusions can be drawn, however, until more cases have been investigated.

SUMMARY

A case of pneumococcal meningitis accompanied by hyperglycemia and successful treatment with chloramphenicol alone is presented. Unusual features were the disappearance of the hyperglycemia with control of meningeal infection and the development of deafness and subdural effusion with relief of the auditory impairment following evacuation of the subdural space.

REFERENCES

1. Hewitt, W. L., and Williams, B., Jr.: New England J. Med. 242: 119, 1950.
2. Recinor, A., Jr., Ross, S., Olshaker, B., and Tribble, E.: New England J. Med. 241: 733, 1950.
3. Kuntz, A.: Autonomic Nervous System, Philadelphia, 1934, Lea & Febiger.
4. Merritt, H. H., and Fremont-Smith, F.: The Cerebrospinal Fluid, Philadelphia, 1938, W. B. Saunders Co.
5. McKay, R. J., Jr., Ingraham, F. D., Morrissette, R. A., Davies, J. A., and Matson, D. M.: New England J. Med. 242: 20, 1950.
6. Smith, M. H. D., Dormont, R. F., and Prather, G. W.: Subdural Effusion Complicating Acute Bacterial Meningitis, read before Society for Pediatric Research, French Lick, Ind., May 10, 1950.

A FATAL CASE OF PNEUMOMEDIASTINUM, SUBCUTANEOUS EMPHYSEMA, AND PNEUMOTHORAX LENTA IN A NEWBORN INFANT

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ALTHOUGH the clinical entity of mediastinal emphysema was described well over 100 years ago by Laennec[1] in his treatise on diseases of the chest, reports of cases in the neonatal period are infrequent and until recently a detailed description of pneumomediastinum was missing from pediatric textbooks.[2-9]

In a very comprehensive paper, Macklin[10] discussed the mechanism of pneumomediastinum and showed conclusively that the pulmonary vascular sheaths were the route of air passage from peripheral sites of ruptured alveoli back to the root of the lung and mediastinum. He noted the effect of progressive interstitial emphysema on the pulmonary blood stream and discussed the so-called "air block." Macklin stressed the importance of the primary pathology-interstitial emphysema because of the ensuing embarrassment to the pulmonary circulation, the spread of infection along the air route, and the possible formation of subpleural blebs which might give rise to pneumothorax.

Since 1941, the literature on pneumomediastinum in the newborn infant has been reviewed by several authors. Gumbiner and Cutler[2] in their report on four cases emphasized the importance of considering pneumomediastinum in the differential diagnosis of neonatal cyanosis and dyspnea. They also demonstrated the importance of lateral roentgenograms in addition to posteroanterior views of the chest as an aid to diagnosis. Lowman and Culotta[6] in reporting three of their own cases pointed out that in each instance some type of artificial respiration had been attempted, in two cases by manual compression of a breathing bag. Heald and Wilder[8] in a review of the literature from 1940 to 1948 reported their successful treatment of the syndrome by needle aspiration.

The clinical manifestations of the syndrome are few. Sudden onset of dyspnea and cyanosis in a newborn infant is the usual history. The findings of a precordial bulge, distant heart sounds, and distended neck veins may be present. The diagnosis can be confirmed by anteroposterior and lateral roentgenograms of the chest.

A recent fatal case complicated by pulmonary hemorrhage and infection was seen at this hospital which presented the clinical and classical roentgenological picture and is reported because of its interesting course and pulmonary pathology.

CASE REPORT

The mother, a 21-year-old Negro primipara, had been seen by a physician only once during gestation. On the morning of Nov. 18, 1949, while at work in the factory where she was employed, she suddenly felt the urge to defecate and went to the toilet where she locked the door. About one hour later, fellow employees found her slumped on the floor and a female infant immersed in the bowl with cord and placenta still intact. The mother stated that she had fainted after what she thought was a defecation. The cord was cut and tied

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and the placenta disposed of by a fellow worker. An ambulance was called, and the mother, who was found to have a third degree laceration of the perineum, was removed to the hospital with the infant.

The infant was first seen in the delivery room at 12:15 P.M. in an obviously critical condition. On examination she was a Negro female neonate, cyanotic, and breathing irregularly at about 80 respirations per minute. Bright red blood-tinged, frothy mucus exuded from the mouth, and a massive subcutaneous emphysema was apparent in the right side of the neck and the posterior scalp region. There was a subconjunctival hemorrhage of the right eye and a marked posterior molding of the head. The heart sounds were slow but regular with a subdued apical impulse in the fourth left intercostal space, mid-clavicular line. The lungs were filled with coarse rhonchi and wet râles throughout.

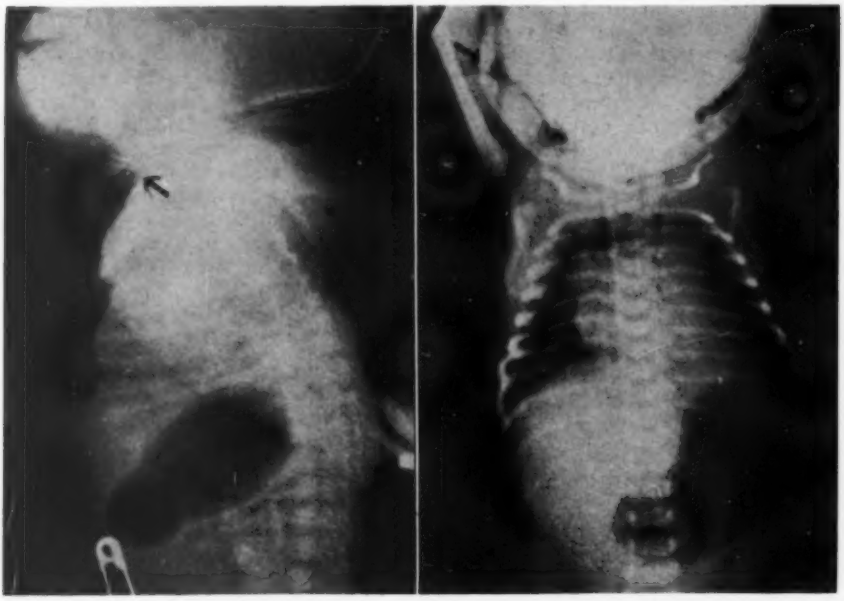

Fig. 1. Fig. 2.

Fig. 1.—Lateral view, approximately six hours after birth, showing submental emphysema.

Fig. 2.—Anteroposterior view, approximately six hours after birth, showing massive emphysema of the neck and the area of increased density in the right upper lobe.

The upper respiratory tract was examined by means of a small laryngoscope and no bleeding point was found, but the same frothy material seen exuding from the mouth was noted in the trachea. The initial impression was (1) subcutaneous emphysema of the neck and scalp, (2) pulmonary hemorrhage, (3) possible pneumomediastinum, and (4) possible intracranial pathology.

The infant was placed head down in a prone position in an incubator under continuous oxygen. Gentle nasopharyngeal suction with a DeLee trap was performed to keep the airway patent. The infant was typed and cross-matched, given vitamin K and prophylactic penicillin 25,000 units immediately and then every six hours. No feedings were given by mouth. Emergency portable x-rays taken in the suspect nursery confirmed the impression of emphysema in the

neck and submaxillary region and in addition showed an area of increased density in the right apex of the lung (Figs. 1 and 2) which appeared to be an area of atelectasis.

For a period of twenty-four hours the infant continued in a critical condition, although under oxygen the color improved, there was relief of respiratory distress, and the heart sounds were stronger. After twelve hours the frothy sputum decreased in amount and changed from the bright red color to a light brown. The lungs continued to show generalized moist râles and a few fine râles at the apices.

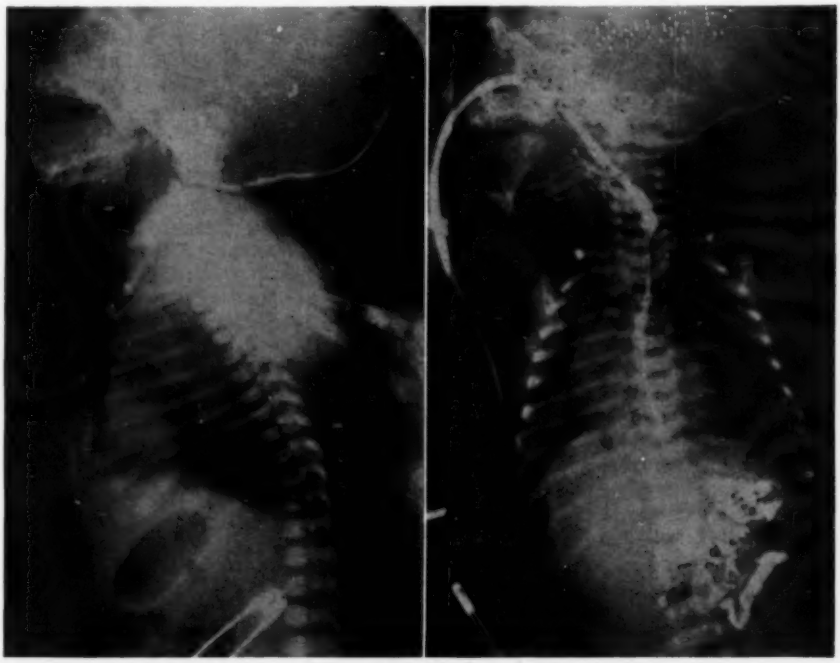

Fig. 3. Fig. 4.

Fig. 3.—Lateral view, twenty-four hours after birth, showing air in the anterior mediastinal space.

Fig. 4.—Anteroposterior view of the esophagram showing the left pneumothorax with mediastinal shift.

The following day the infant was transferred to the Pediatric Ward for further care and x-rays of the chest were repeated (Fig. 3). On admission to the Pediatric floor the infant's weight was 2,960 grams. The blood count revealed 7,410,000 red blood cells, 132 per cent hemoglobin, and 8,400 white blood cells with 19 per cent neutrophiles, 42 per cent metamyelocytes, 37 per cent lymphocytes, and 2 per cent basophiles. Nose and throat cultures revealed only a green pigment producing bacteria which was thought to be a contaminant. The mother's Kahn taken on admission was negative.

For the next forty-eight hours the infant's condition remained unchanged. The lungs continued to show generalized signs but the heart sounds were of better quality and the rate was 96 beats per minute. Hydration was augmented

by clyses in the thighs. By circulating light steam through the incubator, an attempt was made to thin the secretions which had become thicker. On the third day the temperature rose to 39.4° C., the infant seemed slightly more dyspneic, and the impression was that an aspiration pneumonia had become superimposed on the basic pathological picture. Aureomycin, 25 mg. every six hours, was given with antipyretic measures, and the temperature gradually returned to normal after twenty-four hours.

On the fourth day the lung fields appeared to be clearing and for the first time oral feedings of 5 per cent dextrose in saline in 4 and 8 c.c. amounts were offered which the infant took well and retained. However, on the following day when a dilute evaporated milk formula was offered the infant had a paroxysm of gagging and coughing so that oral feedings were discontinued. For the next five days the infant was maintained on parenteral fluids and gavage feedings and her general condition showed a steady improvement. The lungs seemed to be clearing although scattered râles and rhonchi were heard on different occasions. The emphysema gradually subsided, and her color remained good even without oxygen therapy.

Nonetheless, in this interval, several attempts to resume oral feedings had invariably resulted in gagging, coughing, and regurgitation. Because of this and since the infant appeared in good condition, an esophagram was performed in order to rule out the possibility of a congenital tracheo-esophageal fistula or even a traumatic tear of the structures. The esophagus was demonstrated by fluoroscopy to be perfectly normal in contour with no evidence of fistula or obstruction, but for the first time a left pneumothorax was observed (Fig. 4).

In view of the normal esophagram, the infant was again carefully tried on an oral feeding regime. That evening the temperature rose to 38.9° C., and the infant appeared acutely ill. Signs of pulmonary infection reappeared, localized in the right lower lobe. In the twenty-four hours after the esophagram, the infant had taken and retained several oral feedings, but after one of these feedings she regurgitated, apparently aspirated, and turned cyanotic. Immediate response to suction and oxygen was good, but the temperature continued to rise, the blood count showed a leucopenia of 3,150 white blood cells, and the respiratory distress with associated cyanosis increased. The patient expired on Dec. 2, 1949, fifteen days after birth.

Post-Mortem Findings.—The body was opened with the usual "Y"-shaped and intermastoid incisions. The neck organs were normal. By means of a water gutter, whereby water was placed between the skin flap and chest wall and a probe introduced under water, a pneumothorax was demonstrated on the left side. On opening the chest, both lungs were fully expanded; there was no pleural fluid. The mediastinum occupied a normal midline position and was not widened.

The lungs were inflated under water by means of a pump attached to a needle inserted into the closed trachea. Air could be seen bubbling out through a tiny pin-point opening in the left main bronchus. The trachea was normal, and no abnormality was found at the site of the bronchopleural fistula. The left lung weighed 70 grams, the right 90 grams. There was a fibrinous pleuritis present. On sectioning the lungs, many areas of lobular pneumonia were seen scattered diffusely throughout both lungs. In some places these areas of lobular pneumonia were confluent especially in the right apex. The rest of the organs, including the brain, were normal in structure and position.

Microscopic examination revealed the liver to be markedly congested, edema of the interstitial tissue of the thymus, and hyperplasia of the interstitial reticulum cells of the lymph nodes. The lungs showed scattered areas of necrotizing pneumonia with small abscess formation.

DISCUSSION

In the case presented, numerous factors in the etiology of the infant's presenting clinical appearance were discussed. That the delivery must have been precipitous, with a third degree laceration of the mother, was considered likely. What occurred between the time of the birth and the arrival of the intern is not known. The fact that the woman was alone for one hour and that she or someone else might have attempted forcible artificial respiration or, on the other hand, even tried to drown or strangle the infant was considered. Clinically, there was slow steady improvement until the last forty-eight hours before death with gradual subsidence of the emphysema and general improvement in respiration. The occurrence of a pneumothorax at the time when the infant was most improved seemed, however, to precede the rapid downhill course of the last forty-eight hours. The late occurrence of pneumothorax could possibly be explained on the basis of either a sudden rupture of a subpleural bleb or a rupture at the site of the bronchopleural fistula found at autopsy, during one of the episodes of gagging or coughing. Whether early aspiration of the subcutaneous emphysema would have prevented the occurrence of the pneumothorax is questionable since the subcutaneous and mediastinal emphysema subsided and responded to conservative measures. In retrospect, however, it was felt that if the infant had been maintained for a longer period of time on a parenteral feeding regime that the pulmonic infection apparently present but under control by antibiotics might have cleared. It is believed that the immediate cause of death was the sudden obstruction to a limited area of aerated lung field. Since no evidence of trauma or congenital anomalies was found of the upper respiratory passages, esophagus, or stomach, the cause of the continual gagging on oral feedings remains unexplained.

SUMMARY

A fatal case of pneumomediastinum, subcutaneous emphysema, and pneumothorax complicated by pulmonary hemorrhage and infection with post-mortem findings has been presented. The unusual course and problems in its management were discussed.

A review of the literature reveals this to be a comparatively rare condition but one which must be considered in the differential diagnosis of respiratory distress in the newborn infant.

REFERENCES

1. Laennec, R. T. H.: A Treatise on the Diseases of the Chest and on Mediate Ausculation, translated from the third French edition by John Forbes, 1838, Samuel S. & William Wood.
2. Gumbiner, B., and Cutler, M.: Spontaneous Pneumomediastinum in the Newborn, J. A. M. A. **117**: 2050, 1941.
3. Biering, A.: Pneumothorax in the Newborn, Acta Paediat. **28**: 367, 1941.
4. Fisher, J. H.: Spontaneous Pulmonic Interstitial and Mediastinal Emphysema in an Infant, Canad. M. A. J. **44**: 27, 1941.
5. Smith, A. B., and Bowser, J. F.: Spontaneous Pneumomediastinum With Reports of Two Cases in Infants, Radiology **38**: 314, 1942.
6. Lowman, R. M., and Culotta, C. S.: Pneumomediastinum in the Newborn, Am. J. Roentgenol. **53**: 7, 1945.
7. DeCosta, E. J.: Spontaneous Pneumothorax of the Newborn Infant, Am. J. Obst. & Gynec. **39**: 578, 1940.
8. Heald, F., and Wilder, T. S.: Pneumomediastinum in the Newborn Infant, J. PEDIAT. **34**: 325, 1949.
9. Mitchell, A. G., and Nelson, W. E.: Textbook of Pediatrics, ed. 5, Philadelphia, 1950, W. B. Saunders Co., pp. 345-346.
10. Macklin, C. C.: Transport of Air Along Sheaths of Pulmonic Blood Vessels From Alveoli to Mediastinum: Clinical Implications, Arch. Int. Med. **64**: 913, 1939.

Medical Progress

VITAMIN REQUIREMENTS IN ADOLESCENCE

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THE critical role which vitamins play in fundamental metabolic processes renders the establishment of precise quantitative requirements of individual vitamins of great importance.[1] This is particularly true for periods of physiologic and pathologic stress. We were interested therefore in reviewing the data available on the vitamin requirements during the period of metabolic activity associated with adolescence.

Considerable confusion results from the ambiguity customarily associated with the term "adolescence" and with the data obtained in nutritional and metabolic studies in individuals of this age group. Perhaps the most acceptable definition is that suggested by Stuart[2] who considers this broadly as the "period of years between childhood and adulthood." Adequate studies[3] are available which indicate that growth metabolic activities are not uniform during adolescence (Figs. 1 and 2). Of particular importance is the relatively short period of rapid growth characteristic of these years and the individual variations in the age of onset of this growth.[4] The success with which the individual traverses adolescence depends to a considerable extent upon the fulfillment of the metabolic demands during the "growth spurt." With the exception of the studies by Johnston,[5, 6] practically no efforts have been made to define nutritional requirements in the light of individual metabolic variations. In this review we will, therefore, attempt to define vitamin requirements for the rapid growth of adolescence whenever possible.

We do not mean to imply that vitamin requirements of the adolescent have been entirely ignored by physicians, public health officers, nutritionists, and related groups, but there is a paucity of experimental data upon which specific requirements of individual vitamins can be based. Much of the literature presents only dietary surveys and estimates of vitamin ingestion. While such studies have merit, they often lack suitable controls, laboratory quantitation, and close clinical observation of subjects.

Some indication of the prevalence of nutritional deficiencies of adolescent children from low income families has been presented.[7, 8, 9, 10] Results of these surveys indicated that nearly all of those examined manifested one or more mild deficiency states. Since recent studies increasingly emphasize the necessity for the presence of optimal quantities of all nutrition factors,[11] these mild

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Dr. Williams participated in this study while on a Pediatric Fellowship grant by the Provident Medical Associates.

deficiencies should not be minimized. For example, the adolescent may provide for his caloric needs but an inadequate thiamine, riboflavin, or niacin intake may interfere with optimal utilization of the ingested food elements. Since the role of vitamins in carbohydrate[12, 13, 14] and amino acid metabolism[15, 16] has become established, dietary imbalance during the accelerated metabolic activity of this age period assumes greater significance.

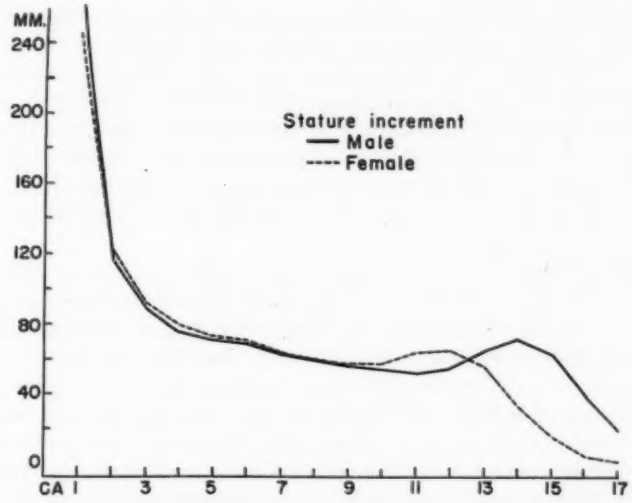

Fig. 1.—Stature increment according to chronological age. (After Simmons.)

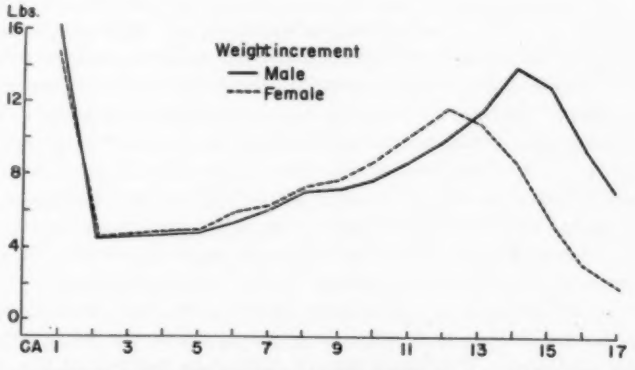

Fig. 2.—Weight increment according to chronological age. (After Simmons.)

This review presents a detailed consideration of the available data on both fat- and water-soluble vitamins and permits an estimate of the daily requirements in the light of present knowledge.

THE FAT-SOLUBLE VITAMINS

Vitamin A.—The estimation of vitamin A requirements is dependent upon physical, physiological, or chemical methods. Chemical techniques for determining plasma vitamin A and carotene are available, but no studies utilizing these methods to evaluate adolescent requirements have been done. Of the several recognized signs of vitamin A deficiency, it now appears that nyctalopia or partial night blindness, is the earliest to appear. While the determination of nyctalopia is useful as a qualitative indication of vitamin A intake, its disappearance under vitamin A therapy does not allow for a quantitative estimate of the optimum vitamin requirements. The amount of vitamin A which will just prevent nyctalopia probably represents slightly less than the minimum requirement. A liberal margin of safety should be allowed for individual physiologic variation and to enable the organism to store adequate quantities during periods of illness or restricted food intake, or during periods of unusual physiologic activity as in adolescence.

Jeans and Zentmire[17] tested 404 country and village school children from 6 to 15 years of age in Iowa and found latent night blindness in 26 per cent of the country children and in 53 per cent of the village children. The highest incidence of night blindness was found in children from families of the lowest income groups in spite of an environment abundant in nutritive foods. A private communication from Jeans and Stearns revealed that the study was done during a year of drought when the gardens failed. Of considerable interest was the finding by these authors that dark adaptation is temporarily decreased during and for a short period after colds, minor illnesses as well as during major illnesses. Observations by Jeans and his co-workers[18] on two 11-year-old boys indicate that 3,000 units of vitamin A daily satisfied their requirements as judged by the biophotometer. This level of vitamin A presumably is suggested, not as the minimal level which would maintain normal dark adaptation, but as an amount which might be considerably above the minimal requirement. Maitra and Harris[19] found definitely subnormal dark adaptation in 30 per cent of 193 elementary school children (from 8 to 15 years of age) in London and Cambridge. Harris and collaborators[20] found that 50 per cent of a group of 760 children 9 to 12 years of age showed hypovitaminosis A by biomicroscopic studies. An enriched dehydrated soup containing the full allowance of vitamins, calcium, and iron in a one-cup serving was given for three months (vitamin A content 4,500 I.U.). Surprisingly the children showed no improvement in vitamin A status as measured by the biomicroscope. Since it is apparent that a diagnosis of vitamin A deficiency is a controversial matter, and because other conditions may give abnormal values, each nutritional survey using the biophotometer must be critically evaluated. The biomicroscope cannot be considered the most valid index of vitamin A deficiency. On the basis of these and other studies the vitamin A requirements are in the range of 3,000 to 6,000 units and the latter figure probably provides for any unusual needs.

Vitamin D.—The data obtained from studies of adolescents indicate that not all individuals are equally efficient in retaining calcium without the ingestion

of vitamin D. Apparently the variability in the capacity to utilize dietary calcium and phosphorus is a major factor in determining the quantity of these elements retained by adolescents as well as by younger children.

Johnston[5] found the daily vitamin D requirement for adolescents to be at least 1,500 units during the period of rapid growth. He also demonstrated that administration of vitamin D (as viosterol) increased the retention of calcium. This study,[22] which was performed on tuberculous adolescents, revealed that the increase paralleled the amounts of vitamin D ingested up to 3,000 units. If this is related to body weight, the quantity of vitamin D necessary for calcium retention in these adolescents was comparable to the dosage for infants. Hence the rapid growth common to both age groups should perhaps be the primary consideration in establishing the vitamin D requirement. Thus the vitamin D requirement during the period of accelerated growth associated with sexual maturation is higher than the 400 units usually suggested as the daily requirement for the adult.

Jeans and Stearns[23] studied fifty children aged 1 to 12 years on varying intakes of milk with and without vitamin D. They observed that if a child utilized calcium efficiently without added vitamin D, its addition to the diet had little effect. If the original utilization was poor, however, the ingestion of additional vitamin D increased the retention of calcium.

Leitch[24] estimated that a retention of from 500 to 700 mg. of calcium daily is necessary to maintain normal calcification during adolescence. Although much work has been done on calcium balance, few workers have studied the influence of vitamin D intake on retention of this element under a variety of dietary conditions. Henderson and Kelly[25] found that the addition of cod liver oil had a variable effect on loss of calcium from the control diet. In one of five adolescent boys, vitamin D had no effect on the loss of calcium, but the others were benefited by the cod liver oil. Insufficient evidence is available on adolescents, but Jeans and Stearns[26] point out that individuals are by no means equally efficient in retaining calcium without ingestion of vitamin D. Whether, in a state of suboptimal calcification, the need is primarily for calcium or for vitamin D is difficult to determine from the data available; it probably reflects the need for both factors.

An impressive report by Follis and collaborators[27] demonstrated the presence of histologic rickets in 107 of 230 consecutive autopsies of children between the ages of 2 and 14 years. The microscopic examination of the middle ribs of these children showed "slight" rickets in 53, "moderate" in 43, and "advanced" in 11 cases. The histologic findings in this study are especially illuminating since profound bony alterations are necessary before characteristic roentgenographic changes make their appearance.

The quantity of vitamin D which may be synthesized as a result of exposure to daylight is not precisely known, but rickets is not uncommon outside the tropical and semitropical zones and especially in cities where much of the sun's ultraviolet radiation is filtered out by smoke. Extensive use has been made of milk fortified with vitamin D, since it provides the vitamin together with an

optimum source of calcium and phosphorus. While the 400 units of vitamin D which are provided in the commercially available quart of fortified milk are adequate for the adult, it would seem wise on the basis of the studies of Johnston and Jeans and Stearns to provide additional vitamin D for the adolescent. The individual variation in calcium retention may exist with low intakes of vitamin D as well as when no vitamin D is ingested. The added stresses of the growth spurt superimposed upon variability in calcium retention would seem to increase the need for vitamin D. We believe, therefore, that 1,000 units of vitamin D per day would more appropriately satisfy the requirement of the adolescent child.

Vitamin E.—Nothing is accurately known of the human requirements of vitamin E. The quantities required by people in good health are unknown because of the difficulty in estimating its presence in food. Symptoms of deficiency are poorly defined clinically. In all probability, if the fat intake is within normal limits the average diet is not grossly deficient unless a defect in absorption of fat is present.

Vitamin K.—It is relatively difficult to produce vitamin K deficiency in mammals by dietary restriction, nor is it possible to decrease sufficiently the endogenous synthesis of vitamin K by microorganisms in the intestinal tract. The oral administration of insoluble sulfonamide drugs does decrease the biosynthesis of this vitamin, but does not entirely sterilize the tract so that it is unlikely that a vitamin K deficiency will be precipitated. Exact requirements are therefore not known at this time.

THE WATER-SOLUBLE VITAMINS

The B group of vitamins is now known to consist of more than a dozen factors, at least ten of which can be obtained in crystalline form. Recent work has defined the function of the individual factors in specific metabolic processes more clearly. Each vitamin probably serves as a coenzyme or as part of an enzyme system concerned in the metabolism of carbohydrate or protein or fat. A few of the well-defined vitamins contained in enzyme systems are thiamine as co-carboxylase, riboflavin in yellow enzyme, niacin in coenzyme I, cozymase or coenzyme II, pantothenic acid as coenzyme A, pyridoxine and pyridoxal in cotransaminase and in codecarboxylase, biotin as cotransaminase, etc. We can look forward to the discovery of additional enzymes which will contain folic acid, para-aminobenzoic acid, and vitamin B_{12}, thereby elucidating the metabolic pathway through which these vitamins act.

Thiamine.—Wilder[28] has pointed out that thiamine deficiency symptoms which develop depend to a considerable extent upon the rate at which deficiency occurs. In all instances the subjects become depressed, irritable, quarrelsome, uncooperative, and fearful. A hyperchromic anemia has also been described in a number of thiamine deficient patients together with bradycardia, diffuse neuritis, and an abnormal electrocardiographic pattern. The thiamine requirements are also directly proportional to the carbohydrate intake as indicated by Elvehjem[29] and Cowgill.[12] Effects of added thiamine upon growth, vision, and learning ability have also been observed. A study[30] to determine

whether additional thiamine over and above that furnished by the daily diet would improve the growth, or vision, or the learning ability in forty-four pairs of identical twins ranging from 7 to 15 years of age showed no significant improvement in the groups receiving a higher intake. This study indicates that there is no value in thiamine supplementation above the levels of intake recommended by the Food and Nutrition Board of the National Research Council.

Benson and co-workers[31] studied the twenty-four-hour thiamine excretion in a group of children aged 4 to 10 years and found that the amount of thiamine excreted was proportional to the amount ingested. The thiamine content of the diet was considered adequate if 25 per cent of ingested thiamine was excreted in the urine. Using this criterion, it was concluded that the thiamine requirement of children of this age group is 0.99 mg. daily. The average daily diet consumed by these children was found to contain 2,159 calories, and the daily thiamine intake averaged 0.990 mg., giving a ratio of approximately 45 mg. per 100 calories.

From a practical point of view, the amount of thiamine recommended for adolescents will necessarily be influenced by several factors, such as quantity of carbohydrate and fat ingested, availability of thiamine synthesized by intestinal bacteria, and, most important, the individual growth increment. However, a reasonably accurate daily allowance of thiamine may be suggested which will fulfill all the metabolic functions during this period of rapid growth. The consensus of available information suggests that this allowance should probably be from 1.0 to 1.8 mg.

Riboflavin.—In 1937 Stiebling,[32] from an analysis of the riboflavin content of diets, calculated the daily intake as follows: boys 7 to 10 years of age 1.2 mg.; girls 8 to 13 years of age 1.2 mg.; other children and adults 1.32 mg. Rose[33] estimated the requirement of the child up to the age of 10 years was 0.88 mg. daily, and adults 0.44 mg. per 100 calories, or 1.1 mg. per 2,500 calories.

The figures for the riboflavin requirement of man may need revision in the light of the studies by Najjar and his colleagues[34] on the human biosynthesis of riboflavin. They demonstrated that riboflavin is synthesized in quantity in the human intestine, and believe that it may not be a dietary essential under all conditions. Thus the recommended dietary levels may be too high. The riboflavin requirements are closely related to body size or more particularly to mass of active tissue, a further fact which may help to explain some of the divergence in vitamin requirements reported for riboflavin.

The dearth of information available on the riboflavin requirement of the adolescent age group makes it all the more important to evaluate critically the recommended allowance for this vitamin. This allowance for riboflavin in 1943 was originally placed at one and one-half times the value for thiamine,[35] but was reduced following a more critical appraisal of the available data in 1945.[36] An abundance of information, much of it unpublished, was obtained during World War II on the vitamin requirement of young men and in general it was concluded that the requirement of thiamine and of riboflavin was approximately equal. This information finds support in the data obtained from extensive experimentation on several laboratory animals. Still another point in

support of the parallel requirement for these two vitamins is found in the close relationship of riboflavin to carbohydrate metabolism and the respiratory enzymes. It appears then that the requirement for riboflavin will be influenced by the same factors which determine thiamine requirement; this may, therefore, be expressed as 0.6 to 0.75 mg. per 1,000 calories, or approximately 1.5 to 2.2 mg. per day.

The latest revision of recommendations by the National Research Council in 1948[37] suggested that riboflavin requirement be based on body weight rather than caloric levels, but this change did not significantly alter the recommended allowances for this vitamin.

Niacin.—It has been indicated previously that there is strong evidence that bacterial synthesis of thiamine and riboflavin occurs in the human intestine. Recently it has been shown by Ellinger, Coulson, and Benesch[38] that niacin is also synthesized by the bacterial flora in the intestine of man, but not to the extent of satisfying the daily requirements.

Recently Bakwin and co-workers[39] observed 225 children with tongue lesions over a four-year period, 60 of which were intensively studied with niacin therapy. While the evidence would indicate that niacin is beneficial in improving the appearance of the tongue, a more critical evaluation of niacin therapy is necessary using other criteria. Again, no specific information is available on niacin studies in adolescents; any estimate of the daily requirement must be speculative in the absence of definitive data. An exhaustive review of the older literature has disclosed no information on the incidence of "pellagra" in the age period under discussion. In spite of the apparently increased demand during this period of growth, the absence of recognizable deficiency signs may perhaps be best explained by general undernutrition with its resultant slowing of growth.

The basis for the figures on recommended allowances for niacin was obtained from experiments with dogs.[40] Available evidence suggests that man has approximately the same niacin requirement per kilogram as the dog. Also, various liver fractions are as curative of blacktongue as they are of niacin deficiency in approximately the same dosage per kilogram. If the growing dog requires 0.25 mg. per kilogram,[26] a boy of average weight (50 to 60 kg.) would require approximately 12.5 to 15.0 mg. of niacin daily. Since the recommended allowance by the Committee on Foods and Nutrition of the National Research Council is ten times that of thiamine, a value of 10 mg. per person per day has often been suggested, but a precise figure for the human niacin requirement has never been determined. In view of the recently demonstrated tryptophane-niacin relationship,[41] it would seem necessary to correlate the niacin requirement with the protein intake, or more correctly with the amino acid content of the diet.

Pyridoxal.—While it has not been proved that the pyridoxine group of vitamins is essential for man, accumulating evidence tends to support the view that it has a definite function in certain aspects of metabolism. The role of pyridoxal in codecarboxylase activity[42] and in transaminase[15] is firmly estab-

lished. Increasing recognition is being given to the role of pyridoxine compounds in the conversion of tryptophane to niacin. Rosen and collaborators[43] were able to show that prolonged pyridoxine deficiency in half-grown rats restricts the transformation of tryptophane to niacin. The metabolic defect was not immediately corrected upon administration of pyridoxine. Subsequent work by Schweigert and collaborators[44, 45] has confirmed and extended the knowledge concerning the relation of pyridoxine to tryptophane metabolism. Because pyridoxine compounds have some value in the therapy of radiation sickness and in some anemias, a more exhaustive survey of the role of this substance in human nutrition is necessary.

The pyridoxine requirement can be considered to be of the same order of magnitude as the thiamine requirement on the basis of animal experiments, and because of its relationship to protein metabolism should undoubtedly be related to nitrogen intake.

Other Factors.—The remaining members of the B group of vitamins are well-defined chemical compounds and, while no definite human requirements have been established, their importance in the metabolic processes of the body cannot be questioned. Pteroylglutamic acid, for example, is conceded to be of primary importance in blood formation, and in both tropical and nontropical sprue. The requirement necessary can only be judged from the quantity administered for therapeutic response, which is from 5 to 15 mg. daily. Inositol is so ubiquitous in plant foods that a deficiency state may never be observed. Biotin has not yet been shown necessary in the normal diet, and the fact that the intestinal bacteria contribute the major portion of the biotin utilized by the host makes it appear that further information is desirable.[46, 47] The need for choline, para-amino benzoic acid, and pantothenic acid has not been definitive enough at this time to warrant the determination of the daily requirement. Vitamin B_{12} is at present receiving much justifiable attention because of its role in hematopoiesis and growth.[48] It is still too early to ascribe a daily requirement for this vitamin.

Ascorbic Acid.—The adaptation of the photoelectric colorimeter for ascorbic acid determination has facilitated quantitative clinical investigation of the requirements for this vitamin. As a result, the literature on ascorbic acid is more abundant.

Minot and collaborators,[49] in a study of 533 children, showed that of the 174 "normal" children in the 8- to 15-year age group, 95 had a serum ascorbic acid level above 0.7 mg. per cent, 79 had a blood level below 0.7 mg. per cent, and 34 were below 0.3 mg. per cent.

Bessey and White[50] studied the plasma ascorbic acid level in children from 5 to 13 years of age but no division into age groups was made, hence the information on adolescents in this study is unavailable. These workers showed, however, that 80 per cent of the children who received the equivalent of 3 ounces of orange juice daily maintained a satisfactory blood plasma level. Roberts and Roberts[51] estimated the vitamin C requirements of five children ranging in age from 7 to 12 years by the administration of a 300 mg. test dose and determined the amount "retained" in the body. This last value, in addition

to the blood concentration, and the response to the test dose were used to judge the state of nutrition of each subject. The three older children, ages 10, 11, and 12 years, required 75 mg. ascorbic acid daily. These workers found that these children required from 1.7 to 2.4 mg. per kilogram to maintain tissue saturation. In a subsequent study, Roberts and collaborators[52] observed 30 preadolescent girls between the ages of 6 and 12 years under well-controlled conditions. Blood levels of 0.7 mg. per cent and an excretion of 50 per cent of the 300 mg. test dose within twenty-four hours were the two indices used to evaluate the vitamin C status. These criteria were used on children receiving intakes ranging from 32 to 82 mg. of ascorbic acid daily. Four-fifths of those receiving 62 mg. per day, and all who received 72 mg. per day, were saturated. The authors infer that between 62 and 72 mg. daily is an adequate allowance for girls between 6 and 12 years of age.

A more direct approach to the adolescent ascorbic acid requirement was employed by Storvick and her co-workers.[53] Reduced ascorbic acid in plasma was determined on 43 boys and 38 girls between the ages of 11 and 18 years. The near fasting plasma values from 0.9 to 1.2 mg. per cent were maintained on diets which provided the allowance recommended by the Food and Nutrition Board of the National Research Council in 1945.[36] There is appropriate evidence indicating that the children under observation in this study were in good nutrition when they received approximately 1 mg. per kilogram.

In a subsequent study, an attempt to establish the ascorbic acid requirements more definitely by analysis of food, plasma, and saturation tests was made. Four girls and four boys, 12 to 14 years of age, chosen from a custodial farm home, were studied under enviable experimental conditions. It was observed that the recommended allowances of the National Research Council (80 mg. per day) maintained all eight children near saturation with ascorbic acid. A survey of all the children between 11 and 18 years of age in this farm home revealed that the diets of even rural children supplied inadequate amounts of ascorbic acid to maintain the blood plasma at an optimum level.

A recent study by this group of workers[54] dealt with the ascorbic acid requirements of 16 college freshmen, most of whom were 18 years old. The results indicated that the daily allowance recommended by the National Research Council, 100 mg. for 18-year-old boys and 80 mg. for 16- to 19-year-old girls, did not maintain the average plasma levels as high as the averages obtained when saturation was obtained with 200 mg. dosages. It was also found that a 70 mg. intake of ascorbic acid was as effective as the 80 mg. intake for maintaining desired plasma concentration. For boys, 90 mg. were as effective as 100 mg. These data appear to support the conclusion that the requirement is approximately 1.3 mg. per kilogram body weight, which is above the 1.0 mg. requirement for younger children.

DISCUSSION

From this review, it is apparent that single or multiple vitamin deficiencies may not be uncommon during adolescence. While this is due in many instances to inadequate intake or improper dietary selection characteristic of many ado-

lescents in our culture, it may also reflect the profound metabolic activities during this period of growth which render the individual more susceptible than ordinarily to a suboptimal diet. It would seem advisable therefore for the physician to suggest an adequate dietary intake with appropriate supplementation to provide fully for the needs of this age period.

In Table I we have listed the allowances of vitamins suggested for adolescents by the Committee on Foods and Nutrition of the National Research Council and a summary of our best estimate of the requirements proposed in the literature. Several surveys[58, 59] have been made on the nutritive value of family diets at various income levels. These studies provide evidence that most of the vitamins are obtained in the dietary of the families of both high and low income groups. As would be expected, the high cost foods (meat, etc.) would be prohibitive to lower income families, and therefore the proteins and B vitamin content of these diets were lower than desirable. It is of interest, however, that in families whose income was $7,500 or over,[58] the protein was 8 per cent lower than the recommended allowance, the calcium 39 per cent, thiamine 24 per cent, riboflavin 15 per cent, and ascorbic acid 8 per cent. While no mention is made of the vitamin D requirement, we can assume that this too is much below the recommended allowance on the basis that the major source of vitamin D was the milk (if homogenized milk was used). If the total quantity consumed furnished 39 per cent less calcium than that recommended, the intake of vitamin D is at least that low. Unfortunately this preliminary report by the Bureau of Human Nutrition and Home Economics provides no information about the age of the children in the families studied. Nevertheless, since vitamin D is present only in small amounts in the diet customarily consumed by adolescents, it should be added to the diet to insure an intake of at least 1,000 units daily, particularly during the phase of rapid growth. The advisability of providing a good source of calcium in the form of one quart of milk has already been emphasized.

TABLE I. SUMMARY OF VITAMIN REQUIREMENTS OF ADOLESCENTS

	ALLOWANCE OF NATIONAL RESEARCH COUNCIL	ESTIMATED REQUIREMENTS FROM THE LITERATURE
Vitamin A	5,000-6,000 I. U.	3,000-6,000 I. U.
Vitamin D	400 I. U.	1,000 I. U.
Thiamine	1.2-1.7 mg.	1.0-1.8 mg.
Riboflavin	1.8-2.5 mg.	0.88-1.32 mg.
Ascorbic acid	75-100 mg.	80-100 mg.
Niacin	12-17 mg.	10 mg.

It is important to evaluate critically much of the published reports on nutritional requirements and of studies dealing with vitamin deficiencies in both animals and man. For example, the lack of adequate correlation between vitamin blood levels and other objective criteria of the nutritional status does not allow for easy clinical assessment of undernutrition. Some workers have recommended determination of the metabolites which increase in the blood or urine during the deficiency. While this may be worth while, it provides only indirect evidence of actual vitamin deficiency. The work of Oldham and

collaborators[55] on the other hand provides direct data since they demonstrated increased blood levels which result from supplementing the diet of children in an institutional environment. Unfortunately, not enough information is available on the vitamin blood levels in normal children of various ages for purposes of comparison.

One of the concerns of those interested in evaluating published data dealing with human nutrition is that a variety of factors may well influence a particular observation. While the intentions and plans of the experimenters are well meant, they are subject to the vagaries of dealing with individuals of different genetic, ethnic, economic, and dietary background. Many of the failings of human nutritional research have been recognized by the Committee on Diagnosis and Pathology of Nutritional Deficiencies of the National Research Council and their report[56] provides an adequate critique of the experimental approach in this field. Notwithstanding the many difficulties, there is a need to obtain data on normal blood levels for the several vitamins, and urinary excretion levels under a variety of dietary conditions.[21] Only with data of this character can it actually be determined whether such vitamin levels have merit in the clinical assessment of the individual's nutritional status. The need for critical evaluation of the biochemical methods employed in nutritional studies has been recognized.[57]

From this review it is evident that little satisfactory data are available upon which to establish optimal vitamin requirements for the relatively brief period of rapid growth in adolescence. Most studies thus far are based upon the prevention of gross deficiencies. There is reason to believe that this does not necessarily correspond with optimal requirements. As a result, the suggested vitamin requirements for the adolescent contained in this review may not be entirely accurate, but they represent the consensus of the best available estimates. It is recommended, therefore, that further studies be undertaken so as to quantitate these requirements with appropriate considerations for the phase of rapid growth in adolescence.

SUMMARY

A review of vitamin requirements in adolescence is presented. Although a planned low cost diet can provide accessory food factors in adequate quantity with the exception of vitamin D, nutrition surveys have revealed the existence of many mild single or multiple vitamin deficiency states. The increased metabolic requirements and the rapid growth spurt characteristic of this age period indicate that an attempt should be made to provide an optimal vitamin intake in the diet or by supplementation. Supplementation of the diet of every adolescent to include 1,000 units of vitamin D daily is specifically suggested.

REFERENCES

1a. Elvehjem, C. A.: The Biological Action of the Vitamins, A Symposium, E. A. Evans, Jr., ed., Chicago, 1941, University of Chicago Press.
b. Green, D. E.: Currents in Biochemical Research, New York, Interscience Publishers.
2. Stuart, H. C.: Normal Growth and Development During Adolescence, New England J. Med. 234: 666-672, 693-700, 732-738, 1946.

3. Johnston, J. A.: Adolescence, Mitchell-Nelson Textbook on Pediatrics, Philadelphia, 1950, W. B. Saunders Co., p. 1587.
4. Simmons, K.: The Brush Foundation Study of Child Growth and Development; II. Physical Growth and Development, Monographs of the Society for Research in Child Development **9**: 1, 1944.
5. Johnston, J. A.: Factors Influencing the Retention of Nitrogen and Calcium in the Period of Growth. IV. The Calcium and Vitamin D Requirement of the Older Child, Am. J. Dis. Child. **67**: 265, 1944.
6. Johnston, J. A.: Adolescence, Brennemann's Practice of Pediatrics, I. McQuarrie, ed., vol. I, chap. 10, Hagerstown, Md., W. F. Prior Co., Inc.
7. Wiehl, D. G., and Kruse, H. D.: Medical Evaluation of Nutritional Status. V. Prevalence of Deficiency Diseases in Their Subclinical Stage, Milbank Mem. Fund Quart. **19**: 241, 1941.
8. Hunt, E. P.: Medical Evaluation of Nutritional Status. VI. Dark Adaptation of High School Children at Different Income Levels, Milbank Mem. Fund Quart. **19**: 252, 1941.
9. Wiehl, D. G.: Medical Evaluation of Nutritional Status. VII. Diets of High School Students of Low-Income Families in New York City, Milbank Mem. Fund Quart. Bull. **20**: 62, 1942.
10. Kruse, H. D.: Medical Evaluation of Nutritional Status, Handbook of Nutrition—A Symposium, J. A. M. A. **121**: 584, 669, 1943.
11. Krehl, W. H., and Elvehjem, C. A.: Imbalance and Dietary Interrelationships in Nutrition, J. A. M. A. **135**: 279, 1947.
12. Cowgill, G. R.: The Physiology of Vitamin B_1, in The Vitamins, Chicago, 1939, American Medical Association.
13. Williams, R. R., and Spies, T. D.: Vitamin B_1 and Its Use in Medicine, New York, 1939, The Macmillan Co.
14. Peters, R. A.: Biochemical Lesion in Vitamin B_1 Deficiency; Application of Modern Biochemical Analysis in Its Diagnosis, Lancet **1**: 1161, 1936.
Peters, R. A.: Pyruvic and Oxidation in Brain; Vitamin B_1 and Pyruvate Oxidase in Brain, Biochem. J. **30**: 2206, 1936.
15. Schlenk, F., and Snell, E. E.: Vitamin B_6 and Transamination. J. Biol. Chem. **157**: 425, 1945.
16. Lichstein, H. C., Gunsalus, I. C., and Umbreit, W. W.: Function of the Vitamin B_6 Group: Pyridoxal Phosphate (Co-Decarboxylase) in Transamination, J. Biol. Chem. **161**: 311, 1945.
17. Jeans, P. C., and Zentmire, Z.: The Prevalence of Vitamin A Deficiency Among Iowa Children, J. A. M. A. **106**: 996, 1936.
18. Jeans, P. C., Blanchard, E., and Zentmire, Z.: Dark Adaptation and Vitamin A, J. A. M. A. **108**: 451, 1937.
19. Maitra, M. K., and Harris, L. J.: Vitamin A Deficiency Among School Children in London and Cambridge, Lancet **2**: 1009, 1937.
20. Harris, R. S., Weeks, Elizabeth, and Kinde, M.: Effect of a Supplementary Food on the Nutritional Status of School Children, J. Am. Diet. A. **19**: 182, 1943.
21. Kruse, H. D.: A Concept of the Deficiency States, Milbank Mem. Fund Quart. **20**: 245, 1942.
22. Johnston, J. A.: Factors Influencing Retention of Nitrogen and Calcium in Period of Growth. III. Puberty in the Normal Girl and in the Girl With the Minimal Re-infection Type of Tuberculosis, Am. J. Dis. Child. **59**: 287, 1940.
23. Jeans, P. C., and Stearns, G.: The Vitamin D Requirements of the Child, Am. J. Dis. Child **54**: 189, 1937.
24. Leitch, I.: The Determination of Calcium Requirements of Man, Nutrition Abstr. & Rev. **6**: 553, 1937.
25. Henderson, J. M., and Kelly, F. C.: Influence of Certain Dietary Supplements in Relation to Calcium Requirements of Growing African Natives, J. Hyg. **29**: 429, 1930.
26a. Jeans, P. C., and Stearns, G.: The Human Requirement of Vitamin D in the Vitamins, Chicago, 1939, American Medical Association.
b. Jeans, P. C.: Vitamin D, J. A. M. A. **143**: 178, 1950.
27. Follis, R. H., Jackson, D., Eliot, M. M., and Park, E. A.: Prevalence of Rickets in Children Between Two and Fourteen Years of Age, Am. J. Dis. Child. **66**: 1, 1943.
28. Wilder, R. M.: Nutritional Problems as Related to National Defense, Am. J. Digest. Dis. **8**: 243, 1941.
29. Elvehjem, C. A.: The Water Soluble Vitamins, Handbook of Nutrition, Chicago, 1943, American Medical Association.
30. Robertson, E. C., Tatham, C. M., Walker, N. F., and Weaver, M. R.: The Effect of Added Thiamine on Growth, Vision, and Learning, Using Identical Twins, J. Nutrition **34**: 691, 1947.

31. Benson, R. A., Witzberger, C. M., and Slobody, B.: The Urinary Excretion of Thiamine in Normal Children, J. PEDIAT. **18**: 617, 1941.
Benson, R. A., Slobody, L. B., Witzberger, C. M., and Lewis, L.: Further Studies On Urinary Excretion of Thiamine in Children, J. PEDIAT. **20**: 454, 1942.
Benson, R. A., Witzberger, C. M., Slobody, L. B., and Lewis, L.: The Blood Level of Vitamin B_1 in Healthy Children and Its Relation to Urinary Thiamine, J. PEDIAT. **21**: 659, 1942.
Benson, R. A., Witzberger, C. M., and Slobody, L. B.: An Evaluation of Blood and Urinary Thiamine Determinations in Vitamin B_1 Sub-Nutrition, J. PEDIAT. **23**: 437, 1943.
32. Stiebling, H. K.: Serial No. R-409, Bureau of Labor Statistics, U. S. Department of Labor, 1936.
33. Rose, M. S.: Laboratory Handbook for Dietetics, ed. 4, New York, 1937, The Macmillan Co.
34. Najjar, V. A., and others: Biosynthesis of Riboflavin in Man, J. A. M. A. **126**: 357, 1944.
35. Recommended Dietary Allowances, Food and Nutrition Board, National Research Council Reprint and Circular Series No. 115, January, 1943.
36. Recommended Dietary Allowances, Food and Nutrition Board, National Research Council Reprint and Circular Series No. 122, revised August, 1945.
37. Recommended Daily Dietary Allowances, Food and Nutrition Board, National Research Council, Revised 1948.
38. Ellinger, P., Coulson, R. A., and Benesch, R.: Production and Release of Nicotinamide by the Intestinal Flora in Man, Nature **154**: 270, 1944.
39. Bakwin, H., Reardon, H. S., Winn, J. S., Tenbrinck, M. S., Stern, M. L., and Engel, M. G.: Relation of Lesions of Tongue in Children to Niacin Deficiency, Am. J. Dis. Child. **74**: 657, 1947.
40. Schaefer, A., McKibben, J. M., and Elvehjem, C. A.: Nicotinic Acid Deficiency Studies in Dogs, J. Biol. Chem. **144**: 679, 1942.
41a. Henderson, L. M., and Hirsch, H. M.: Quinolinic Acid Metabolism. I. Urinary Excretion by the Rat Following Tryptophane and 3(OH) Anthranilic Acid Administration, J. Biol. Chem. **181**: 667, 1949.
b. Henderson, L. M., Ramasarma, G. B., and Johnson, B. C.: Quinolinic Metabolism. IV. Urinary Excretion by Man and Other Mammals as Affected by the Ingestion of Tryptophane, J. Biol. Chem. **181**: 731, 1949.
42. Umbreit, W. W., Bellamy, W. D., and Gunsalus, I. C.: The Function of Pyridoxin Derivatives: A Comparison of Natural and Synthetic Co-Decarboxylase, Arch. Biochem. **7**: 185, 1945.
43. Rosen, F., Huff, J. W., and Perlzweig, W. A.: The Role of B_6 Deficiency in the Tryptophane-Niacin Relationships in the Rat, J. Nutrition **33**: 561, 1947.
44. Schweigert, B. S., and Pearson, P. B.: Effect of Vitamin B_6 Deficiency on the Ability of Rats and Mice to Convert Tryptophane to N'-methyl Nicotinamide and Nicotinic Acid, J. Biol. Chem. **168**: 555, 1947.
45. Junquiera, P. B., and Schweigert, B. S.: Further Studies on the Role of Vitamin B_6 in the Metabolism of Tryptophane by the Rat, J. Biol. Chem. **174**: 605, 1948.
46. Oppel, T. W.: Studies of Biotin Metabolism in Man. I. The Excretion of Biotin in Human Urine, Am. J. M. Sc. **204**: 856, 1942.
47. Oppel, T. W.: Studies on Biotin Metabolism in Man. IV. Studies on the Mechanism of Absorption of Biotin and the Effect of Biotin Administration on a Few Cases of Seborrhea and Other Conditions, Am. J. M. Sc. **215**: 76, 1948.
48. Wetzel, N. C., Fargo, W. C., Smith, Isabel, H., and Helikson, Josephine: Growth Failure in School Children as Associated with Vitamin B_{12} Deficiency, Response to Oral Therapy, Science **110**: 651, 1949.
49. Minot, A. S., Dodd, K., Keller, M., and Frank, H.: A Survey of the State of Nutrition With Respect to Vitamin C in a Southern Pediatric Clinic, J. PEDIAT. **16**: 717, 1940.
50. Bessey, O. A., and White, R. L.: The Ascorbic Acid Requirements of Children, J. Nutrition **23**: 195, 1942.
51. Roberts, V. M., and Roberts, L.: A Study of the Ascorbic Acid Requirements of Children of Early Age, J. Nutrition **24**: 25, 1942.
52. Roberts, V. M., Brooks, M. H., Robert, L. J., Koch, P., and Shelby, P.: The Ascorbic Acid Requirements of School Age Girls, J. Nutrition **26**: 539, 1943.
53. Storvick, C. A., Fincke, M. L., Quinn, J. P., and Davey, B. L.: A Study of Ascorbic Acid Metabolism of Adolescent Children, Technical Bull. 12, Oregon State College, 1947.
54. Storvick, C. A., Davey, B. L., Nitchals, R. M., Coffey, R. E., and Fincke, M. L.: Ascorbic Acid Metabolism of Older Adolescents, J. Nutrition **39**: 1, 1949.
55. Oldham, Helen, Roberts, Lydia J., and Young, Marjorie: Results of Providing a Libernally Adequate Diet to Children in an Institution. III. Blood and Urinary Excretion Studies Before and After Dietary Improvement, J. PEDIAT. **27**: 418, 1945.

56. Kruse, H. D., Bessey, O. A., Jolliffe, N., McLester, J. S., Tisdall, F. F., Wilder, R. M., and Sydenstricher, V. P. W.: Principles Underlying Studies of Nutrition Pertaining to the Influence of Supplements on Growth, Physical Fitness and Health, With a Comprehensive Bibliography of the Studies, Report by the Committee on Diagnosis and Pathology of Nutritional Deficiencies, National Research Council, Arch. Int. Med. **74**: 258, 1944.
57. Jolliffe, N., Tisdall, F. F., and Cannon, P. R.: Clinical Nutrition, New York, Paul B. Hoeber, Inc., p. 127.
58. Nutritive Value of Diets of Urban Families, United States, Spring 1948 and Comparison With Diets in 1942. 1948 Food Consumption Surveys Preliminary Report No. 12, Nov. 30, 1949, U. S. D. A. Agricultural Research Administration, Bureau of Human Nutrition and Home Economics, Washington, D. C.
59. Strauss, M. D., and Reynolds, M. S.: Dietary Practices vs. Food Expenditures in Families Receiving Public Assistance. J. Am. Diet. A. **24**: 490, 1948.

Psychologic Aspects of Pediatrics

THE CHILD WITH TUBERCULOSIS

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THE child with active tuberculosis shows specific psychologic reactions to his disease. This is the conclusion of Dr. Sara Dubo[1] based on a study of twenty-five children on the Children's Tuberculosis Wards at Bellevue Hospital. The behavior is characterized by diffuse motor activity, aggressive outbursts, and an inability to cooperate in the most important aspects of a treatment program. Though the children generally accept without complaint procedures such as injections, pneumothorax, and even major surgical operations, they resist rest in bed and limitation of activity vigorously.

This behavior stems from intense anxiety and deep preoccupations. Much of the thinking of the child with tuberculosis is concerned with death. This motif is prominent in his conversation, his dreams, his fantasies, and his drawings. Sometimes fear of dying while asleep leads to insomnia. Acute depressive episodes, usually of short duration, are common.

Childhood tuberculosis, even when serious, is often symptomless. To the child, his disease is an abstract concept. Nevertheless it is terrifying because he is aware that relatives or friends have died from it. The insidiousness of tuberculosis makes it all the more frightening and threatening. The natural response to danger is increased physical activity, but the child with tuberculosis is expected to be quiet. It is not surprising, therefore, that his fantasies concern themselves with constant motion, such as roller skating, running, dancing, and so on. Conflicts arise in the child because of the desire for activity on the one hand and, on the other hand, the realization that activity tends to spread the disease and prolong the illness.

Regression (reversion to behavior characteristic of a younger age period) is a common reaction in children with chronic illness. It is seen to some extent in tuberculosis, but not to the degree that one might anticipate. The children tend to avoid dependency largely owing to the critical attitude of the group.

Disturbing to the child with tuberculosis is the stress on isolation and precautionary measures. The mask, to be worn when the ward is left for any reason, is especially resented. It is regarded as a stigma and a mark of difference. At the same time there is the feeling that tuberculosis is contracted through uncleanliness and is shameful. Resentment leads to defiance of authority, neglect of precautions, exaggerated sensitiveness to criticism and deprivations, quarreling, and bickering.

Many of the children tend to assume personal responsibility for their illness, blaming themselves for contracting the disease because they "stayed out too late" or "did not obey their parents" or "didn't eat the right food."

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Rorschach responses in twelve children, interpreted by Mrs. Florence Halpern,* showed the following:

Preoccupation with morbid concepts such as death, ghosts, dark aggressive figures.

Extreme, all-pervasive anxiety and depression, efforts at escape or flight.

Marked feelings of inadequacy, insufficiency, and powerlessness.

A turning away from interpersonal relationships. Lack of a real desire for emotional exchange. A seeking for support and reassurance.

Regressive trends.

Feelings of aggression toward what is conceived of as an unfriendly world.

Difficulties in identification.

Many quite normal reactions which are, however, overshadowed by anxiety, depression, and the need for escape.

In regard to therapy Dubo[2] suggests the following:

1. There should be an opportunity on the ward for the development of family constellations with consistent parent substitutes. This is especially important for the younger age group, and particularly the infants.

2. Adequate recreational facilities and opportunities for creative activity should be available to give the child a feeling of social participation.

3. Group discussion, organized along the lines of discussion group therapy, and led by a therapist, will give the children the information about their disease which they need and, at the same time, will allow opportunity for airing and expressing their worries and anxieties. Dubo believes that the usual educational films may do more harm than good.

4. Most important is that the child have the opportunity for positive identification with the adults about him.

REFERENCES

1. Dubo, Sara: Psychiatric Study of Children With Pulmonary Tuberculosis, Am. J. Orthopsychiat. 20: 520, 1950.
2. Dubo, Sara: Personal communication.

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Comments on Current Literature

BACTERIAL "DISPENSERS" IN STREPTOCOCCAL DISEASE

A STUDY undertaken to evaluate the efficacy of triethylene glycol vapor as a means for controlling cross-infections on the wards at Harriet Lane Home yielded extensive data relating to contamination of the environment with hemolytic streptococci and suggested the modes of spread of this infectious agent. Results of this exhaustive investigation, which covered a period from Nov. 1, 1945, to May 27, 1946, are presented in a paper entitled "The Transmission of Hemolytic Streptococcal Infections in Infant Wards With Special Reference to 'Skin Dispersers'" by Clayton G. Loosli, M.D., M. H. D. Smith, M.D., J. Cline, B.S., and L. Nelson, B.S., in the September, 1950, issue of *The Journal of Laboratory and Clinical Medicine*.

In their introduction the authors point up the fact that streptococcal disease manifests itself in a wide variety of illness, such as pharyngitis, tonsillitis, otitis media, cervical adenitis, scarlet fever, erysipelas, and suppurative skin and wound infections. They stress further that this diverseness of clinical manifestations of streptococcal disease (streptococcosis of Boisvert and others) is even more striking in infants and children than in adults. They emphasize especially that streptococcal infections of the skin are quite common in infants, particularly in patients with atopic eczema.

This latter point is significant. The most striking findings of their study concerned the dispersal of a beta hemolytic streptococcus, Group A, Type 33, from a patient with infantile eczema whose skin was shown to be infected secondarily with this strain of streptococcus. This 6½-month-old infant with atopic eczema was admitted to the hospital on Oct. 16, 1945, and was discharged April 27, 1946. The hemolytic streptococcus, Group A, Type 33, was isolated repeatedly from skin lesions and from the nasopharynx of this patient. In the course of the clinical studies it became evident that the presence of the eczematous infant in various locations of the study area determined to a striking degree the number of streptococci in the environment (air, dust, bedclothes, etc.) as well as the extent of infection with hemolytic streptococci in individuals who came in contact with the child. Transfer of this infected patient from one ward to another resulted in a marked clearing of streptococci from the air of the original ward and the extreme contamination of the air in the new ward. These changes occurred within forty-eight hours of transfer.

It was considered of practical significance that adequate treatment of the patient with parenteral penicillin resulted in clinical improvement of the cutaneous manifestations of bacterial infection along with disappearance of streptococci on the skin and in the nasopharynx. Simultaneously, bacteriologic studies revealed that there was prompt disappearance of hemolytic streptococci from the environment (air, dust, bedclothes). As the studies progressed it was clearly shown that secondary streptococcal infections occurred when the ward was highly contaminated with hemolytic streptococci. By careful typing of the streptococci isolated from various sources, it was found that the skin of infected eczema patients and the purulent discharge from ears of patients with otitis media were common and important sources of ward contamination. It

was also found that dried secretions containing millions of streptococci were dispersed into the air and eventually became incorporated into the ward dust, settling on exposed surfaces. The role of contaminated dust was found to be extremely important in the spread of hemolytic streptococci.

The authors conclude that "the path of dispersal of the streptococcus appeared to be from the skin of the infected eczema patients and the pus from the ear of the otitis media patient to the bed clothes, then to the ward air and dust, then to other patients, hospital personnel and visitors." Even when aseptic techniques were meticulously carried out, it was impossible to keep the hands free of bacteria during periods when the dust everywhere contained large numbers of streptococci. Nurses and doctors making rounds first on a ward highly contaminated with streptococci carried the organisms on their so-called "clean" uniforms to other wards.

When skin-infected patients were treated with intramuscular penicillin, 10,000 units every three hours, marked improvement in the oozing lesions was noted, and a simultaneous reduction in the number of organisms isolated from the environment observed. It was shown repeatedly that adequate treatment of bacterial "dispersers" resulted in stopping further contamination of the environment. Although the routine use of aseptic techniques is desirable and must be observed at all times, the present report indicates that such measures failed to prevent the spread of hemolytic streptococci.

The authors conclude that triethylene glycol vapor did not prevent the dispersion of streptococci through the ward. They believe that the role of contaminated dust is important and must be investigated thoroughly. As a practical approach to the over-all problem they suggest the prompt isolation of possible bacterial dispensers, especially the skin dispenser, employment of aseptic procedures, and prompt and adequate treatment of the infected patient with suitable antibiotics. These measures, along with adequate dust control, show promise of providing an effective means for controlling the spread of bacterial infections in hospital wards. Antibiotics employed prophylactically were suggested also as possible means for controlling the spread of secondary bacterial infections to otherwise susceptible individuals.

These principles established for the control of streptococcal disease apply in a similar manner to other important infectious diseases, such as diphtheria, tuberculosis, and pneumococcus infections.

RUSSELL J. BLATTNER.

News and Notes

The **Fifth American Congress on Obstetrics and Gynecology** will be held in Cincinnati, Ohio, March 31 through April 4, 1952. Dr. Fred H. Falls of the University of Illinois will serve as general chairman. The American Committee on Maternal Welfare, Inc., which sponsors the Congress, has moved its office to 116 South Michigan Ave., Chicago 3.

The **American Board of Pediatrics** announces that a written examination will be held under local Monitors on Friday, Jan. 19, 1951, at 2 P.M. This will be the only written examination which will be held during 1951. An oral examination will be held in New Orleans, La., March 2, 3, and 4, 1951.

The following were certified by the **American Board of Pediatrics** at the examination in Chicago, Oct. 13, 14, and 15, 1950.

Dr. Arnold Severen Anderson, 412 Excelsior Ave., Hopkins, Minn.
Dr. Charles R. Baker, 3450 W. 43rd St., Los Angeles, Calif.
Dr. Alfred M. Bongiovanni, 1208 Belfield Ave., Drexel Hill, Pa.
Dr. Vernon Lee Branson, 112 S. 6th, Beatrice, Nebr.
Dr. Mark F. Canmann, 2 N. Sheridan Road, Highland Park, Ill.
Dr. Leon L. Concepcion, Tarlac, Tarlac, Philippine Islands.
Dr. Henry H. Corn, 532 Des Moines Bldg., Des Moines 9, Iowa.
Dr. Peter J. Cotsirilos, 6001 Cermak, Cicero, Ill.
Dr. William Grant Crook, 110 W. Baltimore, Jackson, Tenn.
Dr. Ernest Samuel Cunningham, Jr., 623 S. Henderson, Ft. Worth, Texas.
Dr. Arthur Markham Dalton, 2434 Sylvania Ave., Toledo, Ohio.
Dr. Warren Robert Dammers, 575 Lincoln Ave., Winnetka, Ill.
Dr. Edward Rhiner Doezema, 1419 Waverly Dr., Kalamazoo, Mich.
Dr. Miles Edward Drake, Children's Hospital of Philadelphia, 1740 Bainbridge St., Philadelphia, Pa.
Dr. Emanuel Dubow, 36 Gramercy Park, New York 3, N. Y.
Dr. William Grant Gilger, II, 2024 Schaaf Rd., Cleveland 9, Ohio.
Dr. Helen Martin Gilles, 747 Massachusetts Ave., Lawrence, Kan.
Dr. Richard M. Greenwald, 67-35 Yellowstone Blvd., Forest Hills, L. I., N. Y.
Dr. Walter Moore Hart, 105 W. Cheves Street, Florence, S. C.
Dr. Mark Peter Holland, 27 S. Catawissa Street, Mahoney City, Pa.
Dr. Gerald E. Hughes, 1107 Bryant Bldg., 1102 Grand, Kansas City, Mo.
Dr. George Wallace Kernodle, 305 W. Front St., Burlington, N. C.
Dr. James Absolom Kinder, Jr., 826 Themis St., Cape Girardeau, Mo.
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Dr. C. Ray Leininger, Albert Bldg., 1010 B St., San Rafael, Calif.
Dr. Harold B. Levy, 1727 Line Ave., Shreveport, La.
Dr. Douglas Twichell Lindsay, Public Welfare Board of North Dakota, Bismarck, N. D.
Dr. Ellen Pickard MacKenzie, 33 Fifth St., Gretna, La.
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Dr. Louis B. Silverman, Grand Forks Clinic, Grand Forks, N. D.
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Dr. George K. Stephens, 106 East 13th St., Ada, Okla.
Dr. John Alwin Sterner, 633 Medical Dental Building, Seattle 1, Wash.
Dr. William A. Tanner, 1922 University Ave., Madison, Wis.
Dr. Ben F. Thompson, Jr., 3170 Florida St., Baton Rouge, La.
Dr. Arthur L. Tuuri, Mott Foundation, Children's Clinic, Flint, Mich.
Dr. Douglas L. Wake, 1406 Woodsboro Dr., Royal Oak, Mich.
Dr. Lee Williamson, 1052 North 5th, Abilene, Texas.
Dr. Frank Sum Wissmath, 35 N. Central Ave., Clayton 5, Mo.
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Book Reviews

Communicable Diseases. Edited by Roscoe L. Pullen, Philadelphia, 1950, Lea & Febiger, 1035 pages, 235 illustrations with 20 color plates. Price $20.00.

This rather pretentious volume is written by fifty-three contributors, most of whom are or have been clinicians on the Staff of the Charity Hospital, New Orleans, La.

The diseases have been classified for descriptive purposes somewhat on a clinical basis with reference to the chief localization of the lesions such as those with predominent manifestations in the skin, or respiratory system, or central nervous system, etc. The individual diseases are considered in the conventional manner with somewhat more emphasis on the description of the clinical symptoms than on the possible mechanism of their production. The discussion of the separate infections is usually fairly complete, and each chapter gives a number of references, including some of the most recent publications. Some chapters are more comprehensive than others, and this is especially true of those on rickettsial diseases with which the reviewer was especially impressed. The illustrations in general are excellent and some of the colored plates especially natural. This was particularly true of those illustrating congenital syphilis.

Certain criticisms may be noted. In the chapter on histoplasmosis, for example, too casual mention is made of certain features of much current interest such as the acute infection in infancy, the histoplasmin skin test, and the studies on pulmonary calcification with their epidemiological implications. Also the chapter on scarlet fever should be modernized, particularly regarding specific prophylaxis and serum therapy now only of historic interest, and prognosis which must be modified to fit the fact that now only 100 deaths are reported annually in the United States.

The rationale of including an appendix containing numerous dietary, diagnostic, therapeutic, pharmacologic pediatric procedures in this volume appears questionable.

In general, the broad coverage and the extensive bibliographies of this volume will make it of considerable value for reference. COOKE

The Envelope. James S. Plant, M.D., New York, 1950, The Commonwealth Fund, 299 pages. Price $3.00.

For those familiar with an earlier book of the late Dr. Plant (Personality and the Cultural Pattern), this volume represents a continuation of his study of the relationship of personality and culture. Subtitled "A Study of the Impact of the World Upon the Child," Dr. Plant drew on his long experience in child guidance to probe into the reactions of children to social trends that affect the working through of developmental problems.

Although he considers the child as a part of his environment he postulates a "psychosmotic envelope" between the two which allows for selective interaction. Through a study of the operation of this envelope, as it could be observed in twenty-one different problems frequently encountered in children, it is possible to recognize how the material of the environment is sensed by the particular individual. WARSON

Editor's Column

THE TOXICITY OF VITAMIN A

THE toxicity of vitamins A and D when ingested in amounts many times greater than nutritional requirements has been recognized for some time. Only recently, however, the dangers of prolonged overdosage by lay persons seeking benefits in excess of those that may be derived from prescribed prophylactic dosages of vitamin A have become apparent.

Despite emphasis that the preferred source for the average person's daily intake of vitamins with the exception of vitamin D is from natural foodstuffs and that optimal intakes can be secured from appropriately planned daily menus, there has been a continual increase in the consumption of vitamins from non-dietary sources. There are a number of reasons for this state of affairs which include: (1) widespread emphasis on "luxury" intakes of all known vitamins as a means to a better state of health; (2) the ease of supplementation of natural dietary foodstuffs with the readily available vitamin concentrates, especially the "all-in-one" preparations; (3) extensive newspaper and magazine advertising as well as articles in lay publications stressing the frequency of vitamin deficiencies in the average diet, the ills stemming from such deficiencies, and the cure or prevention of them by single or multiple vitamin preparations; (4) the frequency of prescription of vitamin preparations by physicians for such a variety of reasons as a general improvement in well-being, a substitute for the "tonic" of the previous generation, as well as for an indeterminate number of therapeutic reasons which have little substantiation in fact; and (5) the assumption often by laity and physicians alike that "if a little is good, a lot is better."

The absence of recognized harmful effects from ingestion of excessively large quantities of the water-soluble vitamins with the exception of the transient vasomotor manifestations following large doses of niacin (not niacinamide) and the wide range between the nutritional requirements and the levels of toxic dosages of vitamins A and D have also been important factors in the widespread and ready use of large doses of supplementary vitamins irrespective of the reason for their prescription.

Recent observations indicating that prolonged overdosage of vitamin A is one of the causes of cortical hyperostosis[1] has again focused attention on the toxic dangers of this vitamin. Actually there are not many recorded instances of vitamin A poisoning. Acute poisoning from the ingestion of the liver of polar bears is recognized, with the toxic factor appearing to be vitamin A, which is present in high concentration.[2] It is estimated that 0.5 kg. of polar bear liver contains approximately 8,000,000 units of vitamin A. Acute poisoning has also been rarely observed in children who have ingested the entire contents of a 50 c.c. bottle of Oleum Percomorphum (Bills quoted by Caffey[1]). Principal

emphasis, however, is being placed on the dangers of chronic poisoning. In children fourteen instances have been recorded.[1, 3, 4] In each of these, the symptoms became manifest only after prolonged periods of daily administration of excessively large doses of vitamin A and D preparations. Total daily dosages of vitamin A varied from approximately 75,000 I.U. to 500,000 I.U., and the periods of administration from about six months to two years or more. The probability that vitamin A and not vitamin D or some other substance in the proprietary preparation was the noxious agent is based upon three factors: (1) the dissimilarity of the observed clinical manifestations from those characteristic of vitamin D intoxication; (2) the occurrence of skeletal as well as dermal changes in animals with hypervitaminosis A[5]; (3) the reinduction of the clinical pattern following recovery by Toomey and Morrisette by the administration of vitamin A alone.

The question at the moment would seem to be that of the relative importance of vitamin A intoxication. Literally millions of children and adults are daily ingesting proprietary vitamin preparations as supplements to their dietary intake. The observation of only fourteen instances of chronic vitamin A poisoning during the past six years on the surface would not seem to be very important. Although there have probably been more unrecognized than recognized instances, the clinical pattern is of such an order that, were such poisonings at all frequent, more instances would probably be forthcoming from previously undiagnosed case records. It is significant that all of the recorded instances in children have resulted from overdosage by mothers who have unwittingly assumed that, if small doses were to be helpful, larger ones would be productive of even better results. To date there are no recorded instances of poisoning resulting from the therapeutic administration of large doses of vitamin A. Such a possibility must of course be considered.

Assuming that hypervitaminosis A is not very frequent, what, if any, steps should be taken other than familiarization of practicing physicians with the clinical pattern? Caffey[1] states, "the hazards . . . from the routine prophylactic feeding of vitamin concentrates A and D to healthy infants and children on good diets are considerably greater than the hazards of vitamin A deficiency in healthy infants and children not fed vitamin concentrates." Clausen[6] questions whether healthy children require dietary supplements of vitamin A after they begin to eat vegetables. He has observed that the vitamin A content of the liver increases very little during the first six months of life, whereas there is an increase after this age even though the infant did not receive any dietary supplement of vitamin A. Lewis[7] suggests reduction in the size of the container for proprietary concentrates of vitamins A and D from 50 c.c. to 15 c.c. and a reduction in the concentration of vitamin A to 10,000 units per cubic centimeter (essentially that of vitamin D in the oily preparations; there is a relatively lesser concentration of vitamin A in relation to vitamin D in most water-miscible preparations in comparison with the oily ones). Another suggestion which has been made is to enact federal legislation which would require a warning notice on the label of the vehicle.

It is not the intention to suggest an arbitrary solution at this time, an adequate answer must await further data. Physicians, however, who prescribe vitamin A must be aware of the dangers of overdosage and must warn parents of children and older patients of these dangers. Furthermore, pediatric histories should include, as suggested by Caffey,[1] information relative to overdosage as well as to inadequate intake of vitamins. It would seem obvious that there is need for more precise information regarding the optimal intake of vitamin A at all ages—and one might add parenthetically of its therapeutic value or perhaps more often its lack of it for any of the various conditions for which it is at times prescribed.

W. E. N.

REFERENCES

1. Toomey, J. H., and Morrisette, P. A.: Hypervitaminosis A, Am. J. Dis. Child. **73**: 473, 1947.
Dickey, L. B., and Bradley, E. J.: Hypervitaminosis A: Case Report, Stanford M. Bull. **6**: 345, 1948.
Rothman, P. E., and Leon, E. E.: Hypervitaminosis A: Report of 2 Cases in Infants, Radiology **51**: 368, 1948.
Caffey, J.: Chronic Poisoning Due to Excess of Vitamin A, Pediatrics **5**: 672, 1950.
2. Rodahl, K., and Moore, T.: Vitamin A Content of Bear and Seal Liver, Biochem. J. **37**: 166, 1933.
3. Josephs, H. W.: Hypervitaminosis A and Carotenemia, Am. J. Dis. Child. **67**: 33, 1944.
4. Fried, C. T., and Grand, M. J. H.: Hypervitaminosis A, Am. J. Dis. Child. **79**: 475, 1950.
5. Wolbach, S. B.: Vitamin A Deficiency and Excess in Relation to Skeletal Growth, J. Bone & Joint Surg. **45**: 171, 1947.
Maddoch, C. L., Wolbach, S. B., and Maddoch, S.: Hypervitaminosis A in Dog, J. Nutrition **39**: 117, 1949.
6. Clausen, S. W.: Unpublished data; personal communication.
7. Lewis, J. M.: In discussion of Caffey's paper before the American Pediatric Society, Atlantic City, N. J., May, 1949, and also by personal communication.

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DIABETES MELLITUS IN INFANTS AND CHILDREN

I. Information for Parents

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INTRODUCTION

SINCE the knowledge that your child has diabetes may be very disturbing to you, this material has been prepared to enable you to become more familiar with the condition and to convince you that treatment should be very satisfactory and not too difficult.

As an introduction, it may be called to your attention that effective treatment of diabetes in children has been possible only since the discovery of insulin in 1922. The first insulin to be produced commercially was released in 1923. Before the availability of insulin a child with diabetes could survive only a short time. The condition in some individuals who developed diabetes in adult life, however, was not as severe as that in children and could be controlled often for years without insulin.

Often parents wonder how this condition has developed and why it has occurred in their child. Our present knowledge suggests that the tendency for a person to develop diabetes is inherited. It seems that a parent may transmit this trait to his children without having the disease himself or herself. The tendency is one which has probably been passed down from previous generations, and its presence in no way suggests disease which could have been avoided.

The importance of infection in relation to diabetes is that often the first observable symptoms of the disorder occur soon after an acute infection. Also the diabetic condition in a child usually becomes more severe during the time he has an acute infection.

NORMAL CARBOHYDRATE METABOLISM

It is recognized that when a child has diabetes he has lost his ability to make normal use of the starches and sugars he eats. Therefore, we will consider first the processes that occur in a normal child.

Many articles of food in a diet are carbohydrates (starches or sugars) or contain them in some form. Sugar, for instance, is a pure carbohydrate. Bread, candy, cake, and certain other foods contain much carbohydrate. Certain vegetables and fruits contain more carbohydrate than others. Even meat and protein foods must be considered as contributing to the carbohydrate in the diet. When starches and complex sugars are eaten, certain digestive juices in the saliva and in the intestines act on the food and cause the complex carbohydrates to break down into relatively simple ones which are taken into the blood through the walls of the intestines and brought to the liver and converted

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into glucose or glycogen. In the blood, glucose may be carried throughout the body. In order for the glucose to be used by the body cells, further quite complicated changes must take place. Insulin is necessary for the first of such chemical reactions which begin with the removal of the glucose from the blood. In a child with diabetes this initial reaction does not take place in the normal manner, and glucose accumulates in the blood.

SYMPTOMS AND REASONS FOR THEIR APPEARANCE

There are certain signs and symptoms of diabetes which are very common. The following explanations are given, so that you may understand better the reasons that these signs and symptoms appear.

1. Increased Amount of Urine (Polyuria).—Urine is formed in the kidneys. Certain substances which are carried by the blood are passed into the urine. The appearance of certain substances in the urine depends on the amount that is present in the blood. Sugar (glucose) is one of such substances. Ordinarily the amount of sugar in the blood is low enough, so that sugar does not appear in the urine. In a diabetic child, however, since the sugar accumulates in the blood, sugar is found in the urine. Only a certain amount of sugar can be contained in a certain volume of water, so, as the amount of sugar in the urine increases, the amount of water must increase. This leads to the production of large quantities of urine and loss of water from the body of the child.

2. Increased Thirst (Polydipsia).—As more and more sugar is passed in the child's urine, more and more water is required to be passed too. Therefore, the need of the body for more water increases, and the child becomes very thirsty.

3. Increased Appetite (Polyphagia).—As mentioned earlier, a child with diabetes has lost all or part of his ability to use starches and sugars for food and loses much of the sugar in his urine. Therefore, he does not get from the food he eats the energy for growth and activity that a normal child does. It follows then that the child's appetite increases, and more and more food is eaten.

4. Loss of Weight.—Loss of weight or at least failure to gain weight is almost always found in children with diabetes. There are two reasons for this loss. One is that sufficient energy for growth is not supplied by the child's food since so much sugar is lost in the urine. The other is that such large quantities of water may be passed in the urine that water normally contained in the body is lost, and its weight is lost too.

5. Weakness.—Weakness is a common symptom in a child who has lost much weight.

COURSE OF THE DISEASE IN CHILDREN

When diabetes first is diagnosed, the disease usually is rather mild unless the diagnosis is made during the time the child has an infection. Then the diabetes may be very severe and improve as the child recovers from the infection. The severity of the disease is measured by the amount of insulin it is necessary to give so that a child can use for growth and energy a certain amount of glucose.

Actually a certain amount of insulin is needed for each gram or ounce of glucose which a child eats and changes to energy. If the child's body is able to produce some insulin, less will have to be given. Therefore, the smaller the amount of insulin for a certain quantity of glucose the less severe the diabetes.

The natural course of the disease is that over a period of time the amount of insulin needed for any given quantity of glucose increases. Certain events, such as infection, emotional strain, and overeating, cause the severity of the disease to increase more rapidly, but a gradual increase in severity is to be expected in all cases. This increase in severity usually continues until a child reaches a stage at which it is required that he be given a unit of insulin for every 2 to 8 Gm. of glucose in his diet. In some children this stage is reached in a few months, in others in two or three years. During this period in which a child is progressing to a stabilized state, the severity of the condition may show great variation. In fact some children will improve to such a degree that they will need no insulin at all for a time. As stated before, though, a gradual increase in severity to a stabilized level is to be expected in all cases.

TREATMENT

The chief aim in treatment of diabetic children is to give them as great an opportunity as possible for normal growth and development and normal living. There will have to be certain restrictions and regulations regarding diet. A child whose diabetes is well controlled can be allowed any kind of activity if suitable instructions have been given beforehand.

It is especially desirable that you and your child learn as much about diabetes as possible, so that you will understand the importance of the measures used in treatment. During the first few months of the condition, while you and your child are learning, the disease is less severe than it will be after a year or two. So you have this time to learn before the time comes when mistakes might lead to much more serious results.

Insulin.—Since the body of a diabetic child cannot make the insulin the child needs, it is necessary to supply him with insulin. Insulin is prepared by commercial drug companies and sold ready for use. Insulin is prepared in different strengths, the stronger the insulin the more "units" are contained in a certain volume of the preparation. There are several different kinds of insulin preparations which are listed below:

1. *Regular Insulin* (insulin hydrochloride) has an effect on the body which starts in about one-half hour, reaches its peak in three hours, and is over by six hours.

2. *Protamine zinc insulin* has an effect on the body that starts in about one hour, reaches its greatest in fifteen hours, and is almost over by twenty-four hours.

3. The action of *globin insulin* is between that of the other two, starting in about an hour, reaching its height in six hours, and being over by twelve hours.

Each of these types of insulin is supplied in different strengths known as U-20, U-40, and U-80 insulin, the U-80 insulin being the strongest. (The insulin preparations are named from the fact that there are 20, 40, or 80 units of insulin contained in each cubic centimeter of the preparation.) Insulin dosage is given in units, a certain number of units being recommended for each injection.

To have the effect which is desired, insulin must be injected beneath the skin of the child. In order that this may be done, it is necessary to obtain a syringe into which the insulin can be measured and a needle through which the insulin can be injected.

A syringe is usually made of glass and consists of two parts: a barrel, and a plunger which fits tightly into the barrel. The action of a syringe is very simple since as the plunger is pulled out of the barrel, an empty space is left. If the open end of the syringe is in a watery substance, such as insulin, the substance will flow into the syringe. There are markings on the barrel of the syringe which show the amount of material that has been drawn in.

It is possible to buy syringes marked especially to use with insulin of certain strengths. Thus if a syringe marked to be used with U-40 insulin is used to measure U-40 insulin, the plunger will be pulled out to the mark that measures the recommended number of units of insulin.

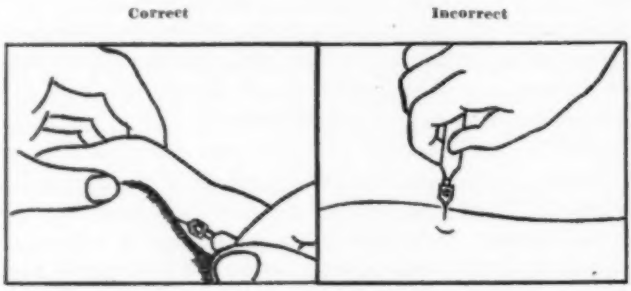


Fig. 1.—*A*, Correct way. Pinch up a fold of skin with thumb and fingers as shown. Hold the syringe parallel to the skin. Insert the needle deep into the fold. The needle should feel loose in the tissue beneath the skin before the injection is given. *B*, Incorrect way. The skin is not lifted up in a fold as shown with correct administration (*A*). The needle is inserted perpendicular to the skin.

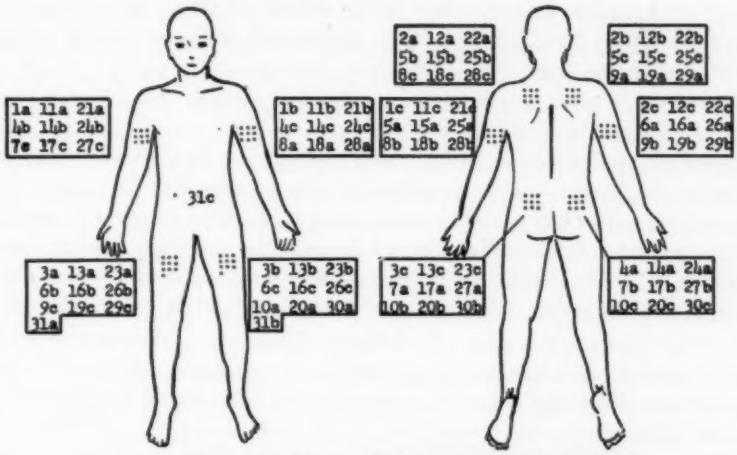
After each use of the syringe and needle, both should be washed in cool water at least five times. Then, in order to prevent infection at the points of injection, the syringe and needle must be boiled for ten minutes in clear water before they are used again. It is suggested that you obtain a covered glass which can be boiled and in which you can keep the syringe.

Insulin should be given where the skin is loose, so that stretching of the tissues and pain will not result.

First a small spot of skin should be cleaned by rubbing it with a piece of sterile cotton which has been saturated with 70 per cent alcohol. Then the person giving the insulin should pinch up a fold of skin with thumb and fingers as shown (Fig. 1). The syringe should be held parallel with the skin. The

If insulin is given once daily, use sites "a".
If insulin is given twice daily, use sites "a" and "b".
If insulin is given three times daily, use sites "a", "b", and "c".
The numerals 1, 2, 3, etc., also refer to the day of the month.

Map for Administration of Insulin to Patient



Map for Administration of Insulin by Patient to Himself

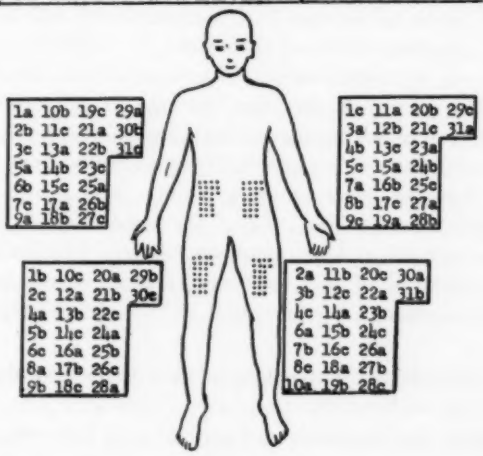


Fig. 2.

needle should be inserted deeply into the fold. The needle should be loose in the tissue beneath the skin before the injection is given.

The type of insulin recommended depends on the condition of the child. Often when a child has developed diabetes recently he is treated with "regular" insulin. If this is the case, he may receive from one to four daily doses of insulin. The best times to give the insulin depend on the child, but usually if only one dose is required, it is given before supper; if two doses are required, one is given before breakfast and the other before supper; if three doses are required, one is given before breakfast, one before lunch, and one before supper; then if a fourth dose is necessary, it is given about midnight.

If a child is given protamine zinc or globin insulin, usually only one injection is required each day.

The same spot for injection of insulin should not be used any more often than necessary in order that the child's skin may be kept in as healthy a condition as possible. This is important because if the skin remains in good condition, the child will have less discomfort from the injection; the appearance of the skin will be normal rather than marred with swellings or pits, and the rate at which the insulin is picked up by the blood will be more uniform.

In Fig. 2 are maps to show how different places may be selected for different doses of insulin. These maps are planned so that even if a child is having as many as three injections a day, the same site will not have to be used again for a period of a month.

In some children the best results are obtained by using a mixture of regular and protamine zinc insulin which is given once a day before breakfast. When this mixture is recommended for your child, you will be told the number of units of each type of insulin to use. One precaution which should be taken in preparing this mixture is that the "regular" insulin should always be put into the syringe before the protamine zinc insulin. The reason for this is that a little of the insulin which is put into the syringe first may get into the second bottle. If, in this way, some of the protamine zinc insulin gets in the bottle of regular insulin, a certain amount of the regular insulin will be changed to protamine zinc insulin, and an unknown mixture will then be in the second bottle. On the other hand, if a very small amount of regular insulin gets into the protamine zinc insulin bottle, it will be changed to protamine zinc insulin, too.

Diet.—A second very important point in the treatment of a child with diabetes is control of his diet.

In this clinic the treatment and care of a diabetic child are based on the principle that good growth can be attained despite the handicap which diabetes represents. Therefore, it is necessary to follow his physical growth and development very closely and to increase the amount of food in his diet as he grows. Then it is possible for the child to grow at the rate he should and reach the final size that he should. Each time a diabetic child attends the metabolism clinic

he is weighed, and his height is measured. These values are plotted on the Wetzel grid for evaluating physical fitness to see whether the rate of growth and direction of growth have been satisfactory. The chart used has three major sections. On the left-hand section you will see numbers of pounds or kilograms of body weight along the up-and-down border. Across the bottom are numbers of inches or centimeters of body height. Then there are physique channels printed diagonally across this section.

To determine the physique or body build of a child at a certain time, the line along the left border which corresponds to his weight at that time is found. Then the line along the bottom border which corresponds to his height at that time is found. The point at which these two lines meet is marked, and the position of this point on the channel system is noticed. When this is done, a point lying in the M channel indicates that the child is of a medium or average build; a point in a B channel that the child is more slender than average; a point in an A channel that the child is stockier or maybe fatter than average. When a child who is growing normally is weighed and measured several times and the points of these values plotted, the line connecting these points goes in the same direction as the printed physique channels, and we speak of the child growing in the right direction.

The second consideration in evaluating the growth of a child is whether or not the child is growing at the best speed. Cutting across the physique channels at regular intervals are lines marked with numbers (0-10-20, etc.) and labelled "developmental level" lines. The developmental level of a child is a measure of his total size, and the value increases as the child becomes larger. Each time a point is plotted using the child's height and weight, the developmental level is determined by reading the value directly.

To determine whether or not the child is growing at the correct speed, the second panel on the grid is used. Along the left border of this section are numbers which designate developmental levels, and along the bottom are numbers which give the age of the child. Each time the developmental level of a child is determined, the line representing this value on the left border is found. Then the line along the bottom representing the age of the child at that time is found. The point where these two lines meet on the chart is then marked. The line joining these points should run in the same direction as the curves printed on the grid.

On the third section of the grid is a scale showing the normal number of calories which boys and girls need to maintain life without growth or activity at different developmental levels (the basal metabolic rates). These values are used in determining the number of calories a child needs in his daily diet, the total calories required for growth and activity of a child being about two times the normal basal metabolism value of the child at his developmental level at the time. You will notice that the basal metabolism values become greater as the developmental level values become greater. Therefore, as your child grows he

requires more calories and, therefore, more food in order to live, grow, and carry on his normal activity.

Sometimes because of illness a child with diabetes will have fallen behind in his growth and development. When this has happened, it is necessary to give the child more than twice his basal calories until he has caught up with the schedule of development that he was following before he became sick. By watching the child's growth and development carefully, the doctor can help the child to grow in a direction and at a speed which is normal for the child.

Therefore, it is planned to give each child a diet which will contain enough of the kinds of food he needs, so that he can grow to his fullest capacity. In order that this can be done, each child is given a diet prepared especially for him. The diet contains food value such that the child can lead an active life and grow his best if his diabetes is controlled well enough for him to get the full use of his food. It is very important that the recommended diets be followed as the child needs the amount of food given to grow his best and because the amount of insulin prescribed is with the understanding that the diet given is the one which is being used. On the diet sheet given you for your child, you will note several letters and numbers at the top of the page.

Following are the explanations of these notations, using the diet sheet (Fig. 3) for examples:

(1) Prot. 104 gives the amount of protein in the child's diet. This is weighed in grams. The number (in this case 104) is the number of grams of protein in the diet.
(2) Fat 156 gives the amount of fat, in grams, which is in the child's diet (in this example 156).
(3) CHO 247 gives the amount of carbohydrate (in grams) in the child's diet (in this example 247).
(4) Calories 2808 tells the amount of energy which the child can obtain from the diet if he eats and is able to use all the food given.

In deciding the number of calories a certain child should have in his diet, his physical status, or his physical condition at the time the diet is given, and his physical progress, or his rate of growth, are both considered. This is done by using the Wetzel grid.

After the total number of calories has been decided, they are divided so that about one-seventh (15 per cent) of them will come from the protein in the diet, half (or 50 per cent) from the fat, and about one-third (35 per cent) from the carbohydrates.

In the example this means that from the protein can be obtained 2808×15 per cent or 421 calories, from the fat 2808×50 per cent or 1404 calories, from the carbohydrate 2808×35 per cent or 983 calories. One gram of protein gives 4 calories of energy, one gram of fat 9, and one gram of carbohydrate 4. So to obtain the number of grams of protein necessary to give the desired calories, the total calories in protein must be divided by 4 ($\frac{421}{4} = 105$); to obtain the

ST. LOUIS CHILDREN'S HOSPITAL

Name NAME OF CHILD History No.

WEIGHTS IN GRAMS

FOOD					PROTEIN 105		FAT 155		CARBOHYDRATE 249		CALORIES
Milk	1200				36		48		60		
Eggs	2				12		10				
Vegetable	2 x 6 gm. CHO								12		
Vegetable	2 x 15 gm. CHO								30		
Fruit	3 x 15 gm. CHO								45		
Cereal	25 gm.				2	1			21	5	
Cream	75 gm.				1	5	14	2	3		
Bread	3 x 50				15				75		
Butter	65						55	2			
Meat	2 x 110				37	4	28	6			
					104	0	156	0	246	5	

NAME OF CHILD
Prot. 104, Fat 156, CHO 247
Calories - 2808
TAG - 322

BREAKFAST

Milk - 400 gm.
Eggs - 2
Fruit - 15 gm. CHO
Cereal - 25 gm.
Cream - 75 gm.
Bread - 50 gm.
Butter - 25 gm.

DINNER & SUPPER

Meat - 110 gm.
Vegetable - 6 gm. CHO
Vegetable - 15 gm. CHO
Bread - 50 gm.
Butter - 20 gm.
Milk - 400 gm.
Fruit - 15 gm. CHO

SCHOOL LUNCH

Meat - 110 gm.
Vegetable - 6 gm. CHO
Fruit - 15 gm. CHO
Bread - 95 gm.
Butter - 20 gm.
Milk - 240 gm.

LIQUID DIET
(one meal only)

Eggnog (Milk - 200 gm.)
(Egg - 1)
(Sugar- 10 gm.)

(Orange juice - 300 gm.)
(Sugar - 10 gm.)

Milk - 300 gm.

(Cream of Wheat - 70 gm.)
(Milk -100 gm.)
(Sugar - 5 gm.)

Fig. 3.

number of grams of fat to give desired calories, the calories in fat must be divided by 9 ($\frac{1404}{9} = 155$); and to obtain the number of grams of carbohydrate to give desired calories, the calories in carbohydrate must be divided by 4 ($\frac{983}{4} = 246$).

(5) TAG stands for "total available glucose."

It has been mentioned that in the process of digestion and that which follows, when the food eaten is used as energy or stored, the carbohydrates are broken down to glucose. It happens that a little over one-half (58 per cent) of the protein and one-tenth (10 per cent) of the fat is also handled as glucose. Therefore, to measure the total glucose available to the body in a diet, the total amount of the carbohydrate food, 58 per cent of the amount of protein, and 10 per cent of the amount of fat are added. In the example, this is:

58 per cent protein =	60.9
10 per cent fat =	15.5
100 per cent carbohydrate =	246.0
	322.4 Gm.

For a child to lead a normal life, he must be allowed to enter occasionally into certain unusual activities. It is usually possible, on special occasions, to obtain from the dietitian certain substitutions of food which may be used in order that the child can take part in the special activities. Until you have had a great deal of experience with handling your child and his diabetes, however, do not try to make these substitutions yourself.

In order that the progress of a child at home may be followed closely, there are certain records which should be kept. These records have been designed to give the doctor the information he needs to make recommendations for care of the child. Probably, at first, you will be asked to keep a complete record every day. Then later it may be possible for enough information to be obtained by keeping complete records only on certain days.

A copy of the record sheet (Fig. 4) and explanations of the headings of the columns follow:

(1) *Date:* day, month, and year for which record is being kept.

(2) *Time:* This gives the time interval during which a certain urine specimen is being collected in the bladder. To start the record, have the child void his urine, and enter the time that this specimen was voided (for example, 3 P.M.). On the next line enter the same time (3 P.M.) with a dash following. The next time the child passes his urine, enter this second time (for example, 5:30 P.M.) following the dash on the second line. This urine will be that which collected in his bladder between 3 P.M. and 5:30 P.M. Enter 5:30 P.M. on the third line and continue in the same manner.

(3) *C.C.:* In this column is the record of the amount of urine passed each time. Rather than make the measurements in ounces and quarts, you are asked to measure in cubic centimeters or "c.c.'s." Tubes or bottles with this unit of measurement marked on them can be bought. They usually are glass and have marks and amounts on the sides much as on a measuring cup.

Each time the child passes urine, it should be collected in the measuring bottle and the amount (for example, 250 c.c.) entered in the column on the line which gives the time this urine was collecting in the bladder.

(4) *Glucose (per cent):* In this column is listed the per cent of sugar in each urine specimen. To find the per cent present in a specimen, a test is done using a special testing set called a Sheftel set. The test is done according to the directions with the set. Then the per cent of sugar in the sample (for example, 3 per cent) is entered in the column.

(5) *Glucose (Gm.):* The amount of glucose in each sample is determined by multiplying the volume of the urine by the per cent of glucose. The amount is expressed in grams which is a unit of weight. In the example given, this would be 250 × 3 per cent or 250 × .03 = 7.5 Gm. At the end of each twenty-four hour period, a total is obtained by adding the separate values.

DIABETIC OUT-PATIENT RECORD OF Name of Patient C.H. #
O.P.D.#

(1) Date	Urine (2) Time	(3) C.C.	(4) Glucose Per Cent	(5) Glucose Gm.	(6) T.A.G. Gm.	(7) G.M. Gm.	(8) G/I	(9) $FeCl_3$ Test	(10) Insulin Units	(11) Remarks (Infections, reactions, changes in diet, etc.)
5-3-49	1 p.m.	150	2	1.0						returned home from hospital
	3p.m. - 5:30p.m.	250	3	7.5						
	5:30p.m. - 7p.m.	500	1	5.0						
	7 p.m. - 9 p.m.	200	1/2	1.0						
	9p.m. - 12 M	300	1/2	1.5						
	12 M - 6:30a.m.	350	0	0						
5-4-49	6:30a.m.-9 a.m.	250	1/2	1.2					12 regular 12 PZ mixed	
	9a.m. - 11 a.m.	200	1	2.0						stayed home from school and read quietly
	11a.m.-12:30p.m.	175	1/4	1.4						much of the day
	12:30 p.m. - 3:30 p.m.	250	2	5.0						
	3:30p.m.-6 p.m.	400	1/2	2.0						
	6 p.m.-9 p.m.	300	1	3.0						
	9 p.m.-1 a.m.	250	1/4	0.6						
	1 a.m.-6:30a.m.	300	0	0						
	TOTAL			18.2	190	190 - 18.2 = 171.8	172 ÷ 24 = 7.1		24	

Fig. 4.

(6) *T.A.G. (Gm.):* This figure need be entered only once a day. It is marked on the diet sheet and is explained previously.

(7) *G.M. (Gm.):* In this column, too, an entry is made only once a day. Usually the day is measured from 7 o'clock one morning until 7 o'clock the next morning.

G.M. (Gm.): stands for grams of glucose metabolized. This measures the amount of glucose taken in the diet which is used by the child's body for either energy or storage. The number is obtained by subtracting the grams of glucose lost in the urine, the total for twenty-four hours in column 4 from the total amount taken in the diet, the T.A.G. from column 6.

(8) *G/I:* This value is figured only once every twenty-four hours. It is called the operating glucose insulin ratio and indicates how much sugar in the diet is taken care of by each unit of insulin given. The G/I ratio for a twenty-

four hour period is found by dividing the grams of glucose metabolized (column 7) by the total number of units of insulin given during the twenty-four hours.

(9) *$FeCl_3$ Test:* This test need be run on a urine specimen only when two specimens in succession have contained at least 2 per cent sugar. This test is done by putting urine in a test tube to a level of about an inch. Then a solution of ferric chloride is added drop by drop. At first the liquid in the tube will become cloudy. If the test is positive, the solution will then clear and become a purplish-red color. All other results are recorded as "negative." If this test is positive, it indicates that the child's metabolism is more severely involved than usual, and the doctor should be notified.

(10) *Insulin Units:* Enter each dose of insulin in this column on the line which indicates the approximate time that the insulin was given. In recording insulin, tell the number of units given and the type of insulin used (for example, "r" for regular, "pz" for protamine zinc, etc.). If mixed regular and protamine zinc insulin is used, give units of each.

(11) *Remarks:* Under remarks, note anything about the child which is unusual, such as an unusually active day or a very quiet day, a cold, fever, illness of any kind, headache, insulin reaction, change in diet. Knowledge of all these things will help in directing the treatment of the child.

INSULIN REACTIONS

Under certain conditions, insulin given to a child may be more than he needs to use the sugar in his food on that particular day. When this occurs, sugar may be removed from the blood until the amount left in the blood is below the normal amount. When this happens, a child's body will react in a certain way according to the child and according to the amount of the sugar in the blood. Some of the signs which may be expected are pallor, sweating, inability of the child to respond as well as usual, inability of the child to see as well as usual, irritability, hunger and, finally, in severe conditions, convulsions. The symptoms do not appear in the same order in all children but usually appear in the same order in the same child. So it is often possible for a child to realize that he is starting to have a reaction and either treat the condition himself or ask his parents to do so.

The treatment of an early insulin reaction is very simple. If it is almost time for a child to be given a meal, the easiest treatment is to feed him his meal a little early. In case the child is receiving a dose of regular insulin before each meal, the dose should be delayed until after this meal and a slightly reduced dose given. If the mild reaction occurs at another time of day or night and the child is able to take food by mouth, he should be given orange juice with sugar in it. The amount depends on the size of the child.

TABLE I.—AMOUNT OF ORANGE JUICE AND SUGAR WHICH SHOULD BE GIVEN FOR A MILD INSULIN REACTION

BODY WEIGHT OF CHILD		AMOUNT OF ORANGE JUICE		AMOUNT OF SUGAR TO BE ADDED
Kilograms or Pounds		c.c. or	oz.	Teaspoonfuls
10	22	60	2	0
20	44	120	4	0
30	66	180	6	0
40	88	240	8	0
50	110	240	8	1
60	132	240	8	3

If, before it is recognized that a child is developing an insulin reaction, the reaction becomes severe and the child is not able to take food or liquid by mouth, a different type of treatment is needed. You should always have available a small vial of 1:1,000 Adrenalin or epinephrine. If your child develops a severe insulin reaction, measure into the insulin syringe an amount of Adrenalin according to the size of the child. The doctor will have told you the amount proper to use in case of such emergency. Then, holding an area of skin of the arm or leg firmly, insert the needle straight into the child's arm or leg, and inject the Adrenalin. Response to this treatment will not follow immediately, but should be seen in ten to fifteen minutes. During this time, prepare a suitable amount of orange juice and sugar for the child, so that this can be given when the child is able to take it by mouth. Then if the reaction was severe, call the physician who has been following your child.

Insulin reactions may occur during a phase when a child's diabetes is improving rapidly, such as after recovery from an infection. During such times, it may be necessary to reduce a child's insulin rapidly, and the child should be under the supervision of his physician.

Also when a child is more active, he requires less insulin to use a certain amount of glucose. Therefore, if you know your child is to have a day of definitely increased activity, he should have either a smaller dose of insulin or an increase in diet on that day. Your doctor will advise you regarding the amount the insulin should be reduced or the amount the food should be increased.

Infection.—Since the severity of the diabetes is usually rapidly and greatly increased when the child has an infection, you should always notify your doctor when your child has a fever or seems sick. Then you can be guided in proper treatment during this time.

You will notice that on the diet sheets given to you there is listed food for a one-meal liquid diet. At times it may be necessary to substitute this food for the child's regular solid food. Usually, at least until you are familiar with the treatment of diabetes, your physician should be notified if you think this substitution desirable. He can then advise you regarding further treatment.

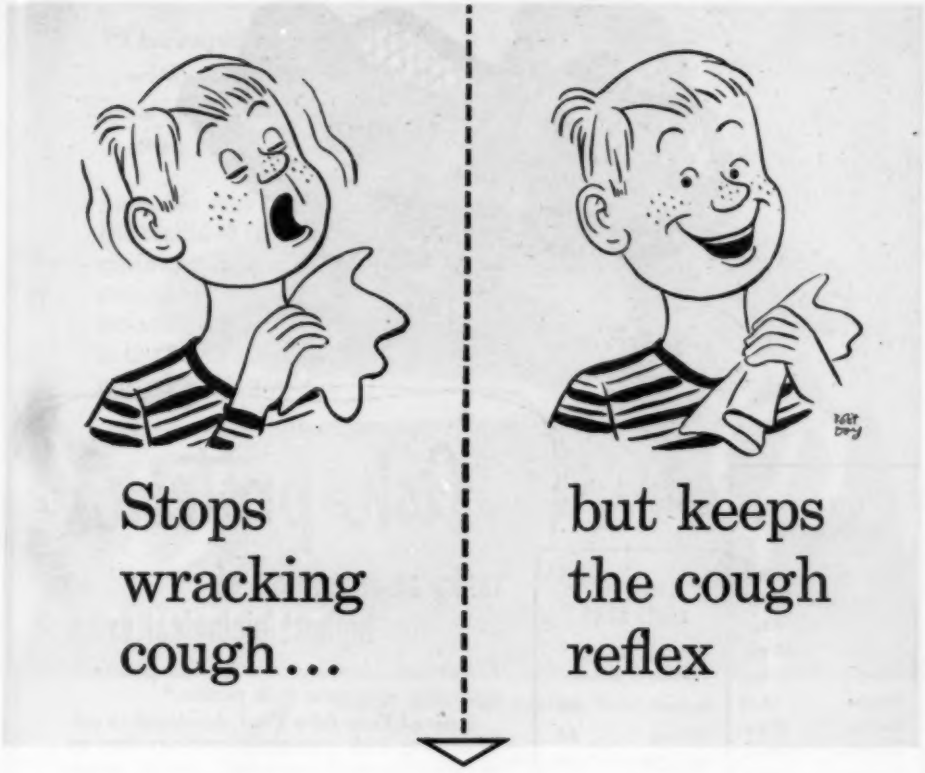
REGULAR VISITS TO THE DOCTOR

From the time that you are told that your child has diabetes, it is important that you take him regularly to the physician who is to help you supervise his care. In this way both you and the child will have some help and guidance during the early less severe stages of the diabetes and become more acquainted with the disease before it reaches such a severe stage that strict control is very necessary. Also both you and the child will become acquainted with the physicians, the nurses, the social workers, the dietitian, and others who work with you.

Then, if an emergency arises or if you or the child have a special question to be answered, you will know where to go for help. You may find that you will want some help in interpreting diabetes to your child and in directing him to follow recommendations made for his care. Certain problems in understanding

arise which vary with the child and with his age. It is best to consider each of these problems as it arises, and a doctor can do that much better if he knows you and your child beforehand. Also, since the same problems seem to arise in many instances, your physician can often help you to anticipate and avoid some of the situations which can occur and which can make it difficult to keep your child regulated the way that is best for his physical condition.

It is advisable, too, for you to take your child to the physician regularly because periodically certain increases in diet and in insulin are necessary in order that the child may obtain enough energy to grow and develop to his fullest capacity.



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Niacin	12 mg
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(Values given as percent of protein)

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Histidine	5.7
Isoleucine	4.7
Leucine	7.0
Lysine	8.3
Methionine	2.8
Phenylalanine	3.5
Threonine	4.1
Tryptophan	1.1
Valine	5.2

*Dunn, M. S.: The Nutritional Value of Fish Proteins, Institute of Food Technologists, San Francisco meeting, (July) 1949. Geiger, E., Nutritive Value of Fish Protein, Progress in the Chemistry of Organic Natural Products, Ed. by L. Zechmeister, 5:275, 1948.

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[1]Hansel, F. K.: Ann. Allergy, 1:199-207, 1943

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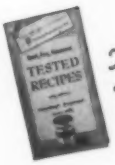
[1]Gamble, J. A.; Ellis, N. R. and Besley, A. K., U. S. Dept. of Agric. Tech. Bull. No. 671, page 61, (March 1939).



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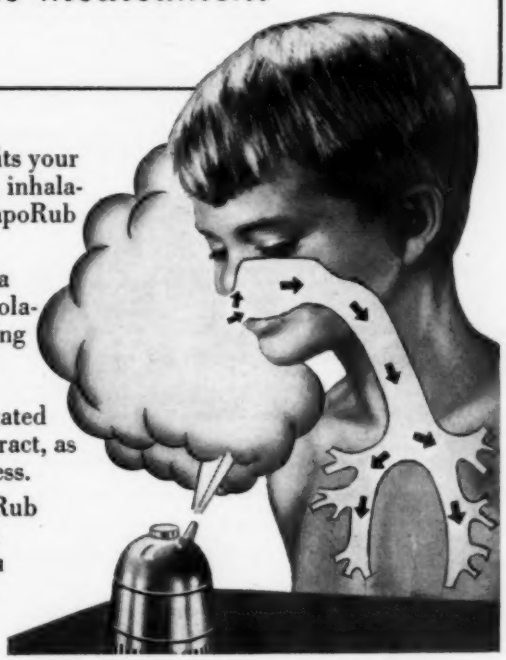

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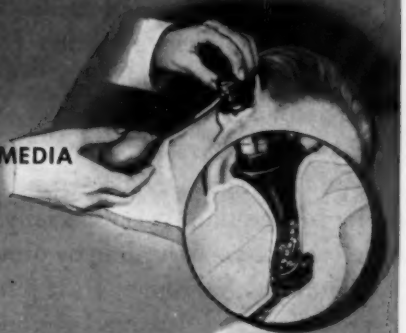

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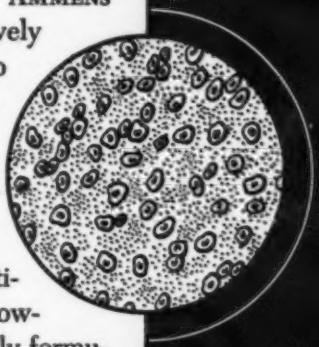

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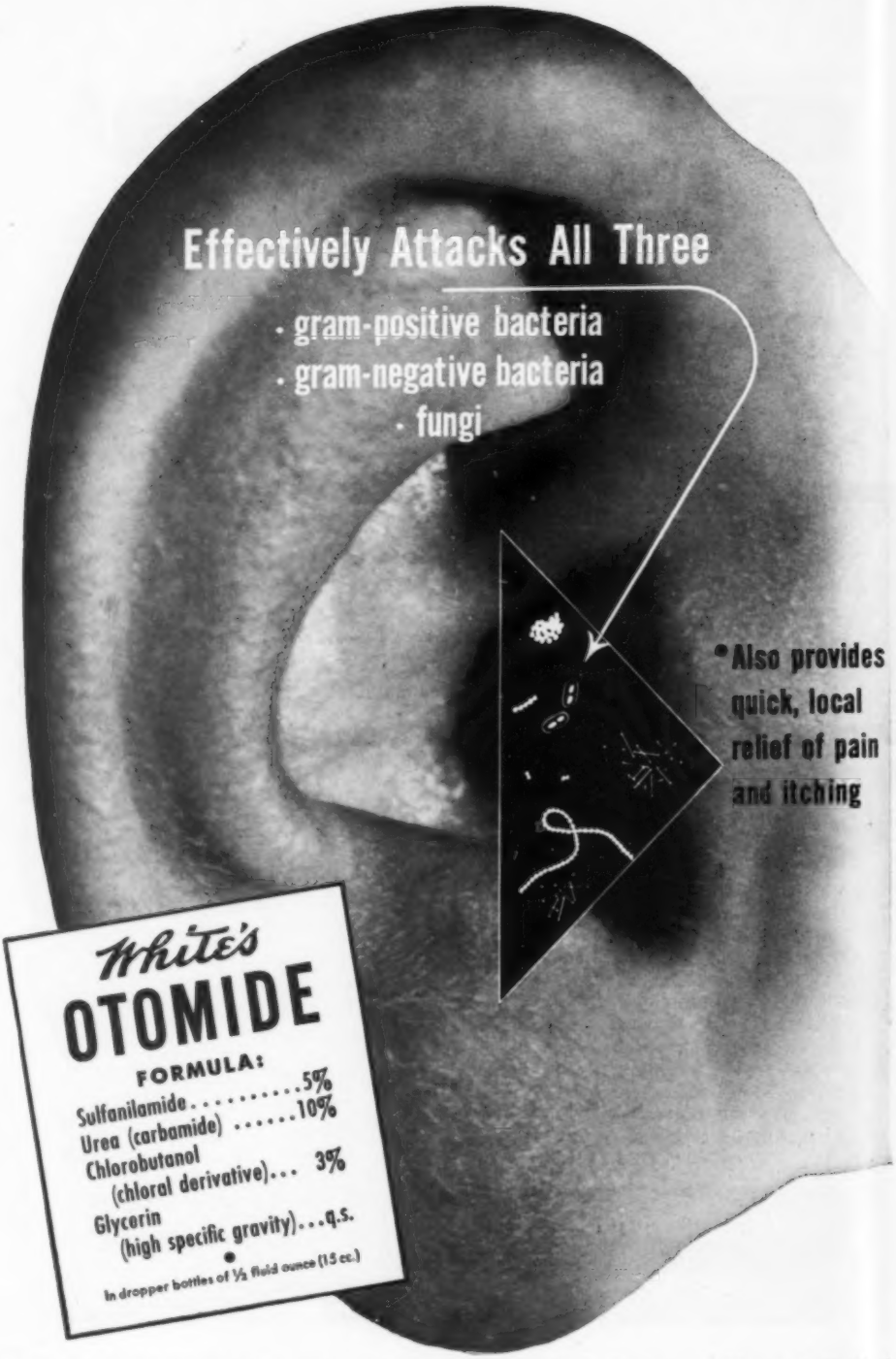

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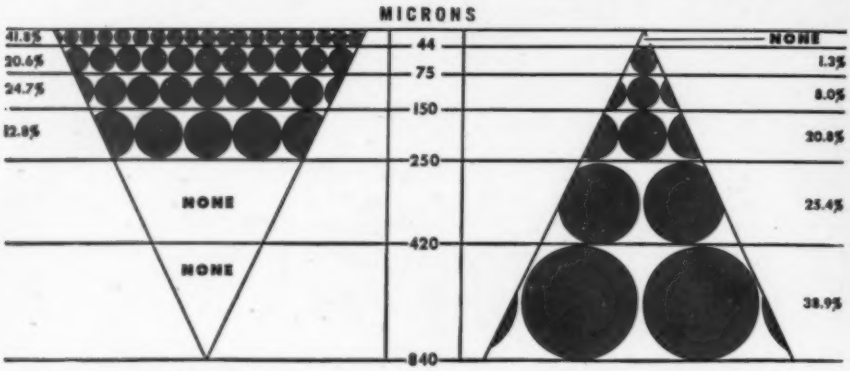
1. Stoll, Norman R.: Jrl. of Parasitology 33:1 No. 1 (Feb.) 1947.

Particle Size

AN INDEX TO READY DIGESTIBILITY



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keep cough within bounds with

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By its dual action, local and central, DIATUSSIN reduces irritation of respiratory tract mucosa, liquefies mucoid secretions and raises the cough center threshold to excessive stimuli. DIATUSSIN thus lessens the frequency of cough, enhances its efficiency and transforms it from the irritating dry type to the easier productive type. It does not suppress cough, as narcotics may do, but keeps it under control, and makes it useful rather than harmful.

Administration: Orally, for children 2 to 5 drops, or 1 to 2 fluidrams of syrup, repeated as indicated; for adults 7 drops, or 1 tablespoonful of syrup.

Supply: DIATUSSIN Syrup—Each fl. dr. (3.7 cc. teaspoonful) contains 2 drops of the extract—Bottles 4 fl. oz., 1 pt. DIATUSSIN—Vial, 6 cc.

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UNICEF—International Supplier

• In December, 1946, the U. N. General Assembly by unanimous vote created the United Nations International Children's Emergency Fund and charged it with one responsibility: to aid the world's needy children. At first, the Fund concentrated its resources and energies toward alleviating desperate emergencies caused by the war—helping the maimed, orphaned, sick and plain hungry children. The Fund still answers emergency calls, such as, aiding one-half million refugee children and mothers in the Near East, helping the child victims of the earthquakes in 1949 in Ecuador, in 1950 in Assam, India. But its work is gradually passing from emergency aid to long range programs that will help countries give their children a happier, healthier future.

• What kind of assistance does UNICEF give? It provides food for supplementary feeding; raw materials for the manufacture of clothing, blankets and shoes; services and equipment for baby clinics and child care institutions; medical supplies, transport, insecticides and sprayers for medical programs; and up-to-date training of pediatricians, nurses and child health workers.

• One of the most important phases of the health program is BCG (Bacillus Calmette Guerin) anti-tuberculosis vaccination campaign. The goal set for this campaign is the testing of 50 million children and the vaccination of all non-reactors. To date the campaign has reached 27 million children.

• Other diseases are being fought just as systematically. In India, for example, more than one death in three comes from malaria. So UNICEF has been supplying DDT to spray huge areas to stamp out this plague. In Italy, thousands of children and adults have been treated for the cure and prevention of venereal diseases. In China, classes have been held to teach rudimentary sanitation to midwives who in that land of few trained doctors have for centuries delivered the children of China.

• The slow, steady and unheralded progress of these UN health and child welfare programs are the positive side of the post war effort toward peace. Some of the money that has made it possible has come from government treasuries; more of it has been contributed by the people in many lands. To cite a few instances, voluntary citizens' campaigns have just been completed in Canada and the Dominican Republic and are now under way in New Zealand, Belgium, Austria, Italy, Yugoslavia and Australia. *People in the United States can do their part to aid in this world-wide humanitarian work by forwarding their contributions to the U. N. Children's Fund Committee, New York 16, New York.*

For Patients Allergic to Eggs, Wheat and Milk

BANANA RYE BREAD

(Egg, milk and wheat free)

2 cakes or packages yeast
¼ cup warm (not hot) water
1 tablespoon salt
1½ tablespoons sugar
2 tablespoons melted vegetable shortening
2¼ cups mashed ripe bananas* (5 to 6 bananas)
5¼ to 6 cups rye flour

**Use fully ripe bananas . . . yellow peel flecked with brown.*

Dissolve yeast in water. Mix together salt, sugar, shortening and bananas. Add half the flour and beat until smooth. Beat in the dissolved yeast. Add remaining flour gradually and mix well.

Turn dough out onto a floured board. Knead about 8 minutes, adding just enough additional rye flour to prevent sticking. Place dough into a lightly greased bowl. Cover and let rise until double in bulk (about 2 hours).

Turn out again onto floured board and knead lightly about 2 minutes. Shape dough into 2 loaves. Place into lightly greased bread pans (8 x 4 x 3 inches). Cover and let rise again until double in bulk (about 1 hour).

Bake in a hot oven (425° F.) 5 to 10 minutes, or until crust begins to brown. Reduce temperature to 350° F. and bake 35 to 40 minutes longer, or until bread is done. Remove from pans. Brush top crusts with water. Makes 2 loaves.

All measurements used in this recipe are level.

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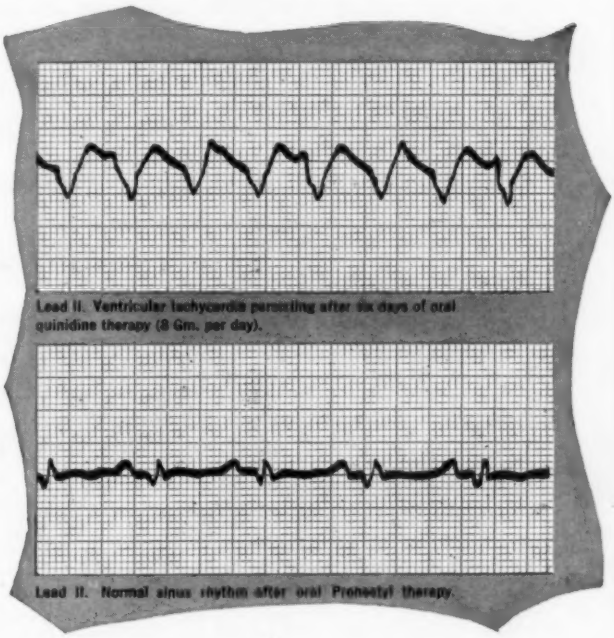

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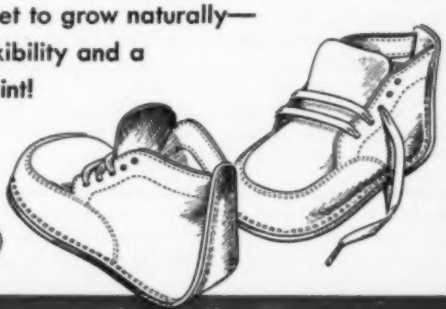

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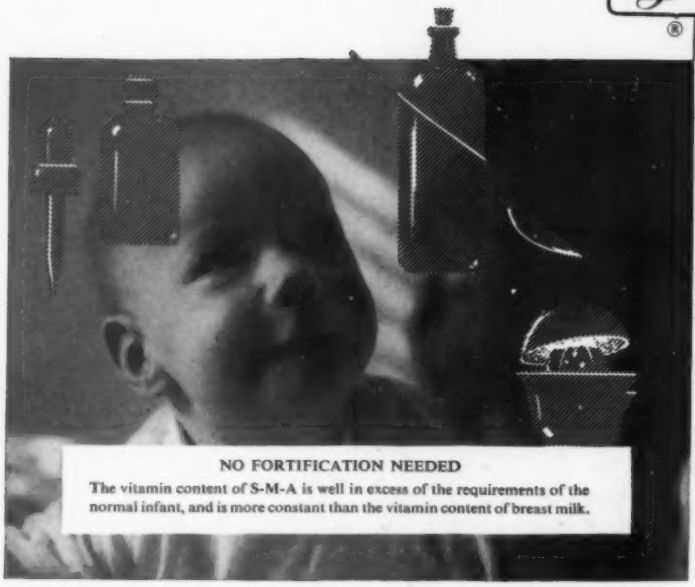

NO FORTIFICATION NEEDED
The vitamin content of S-M-A is well in excess of the requirements of the normal infant, and is more constant than the vitamin content of breast milk.

A Complete, Protective Infant Food . . .

S-M-A, diluted and ready to feed, provides in each quart the following proportions of the minimum daily requirements for infants.

VITAMIN A 5,000 U.S.P. units	333%
VITAMIN D 800 U.S.P. units	200%
THIAMINE 0.67 mg.	250%
RIBOFLAVIN 1 mg.	200%
VITAMIN C 50 mg.	500%
NIACINAMIDE 5 mg.	–

Ready-to-feed S-M-A is the most complete formula for infants. Its protective vitamins are administered in the most satisfactory way—right in the food and in each feeding. No danger of forgetting, no extra burden for busy mothers.

No infant food is more like breast milk than S-M-A—in content of protein, fat, carbohydrates and ash, in chemical constants of the fat and in physical properties.

S-M-A CONCENTRATED LIQUID—cans of 13 fl. oz.
S-M-A POWDER—1 lb. cans

S-M-A®

vitamin C added
builds husky babies

Wyeth Incorporated, Philadelphia 3, Pa.

exercise in simple logic

Combined sulfonamide mixtures are more desirable than single sulfonamides. Mixtures of three drugs offer advantages over mixtures of two drugs. Sulfadiazine and sulfamerazine deserve first and second place respectively in any mixture.

"Sulfacetimide appears the most advantageous for third place."[1]

TRICOMBISUL

is more desirable and offers many advantages in sulfonamide therapy.

TRICOMBISUL: Tablets 0.5 Gm., each containing 0.166 Gm. sulfa*cetimide*, 0.166 Gm. sulfadiazine and 0.166 Gm. sulfamerazine. Available in bottles of 100 and 1000 tablets.

1. Lehr, D.: Scientific Exhibit, Atlantic City Session, American Medical Association, June 6-10, 1949.

*T.M.

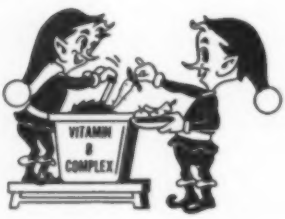
Schering CORPORATION

SCHERING BLOOMFIELD, NEW JERSEY

TRICOMBISUL

QUESTION: *How many red blood cells are replaced due to "wear and tear"?*

ANSWER: *Approximately 25 million a day in normal people*



When abnormal demands overtax the blood forming capacity of the body producing easy fatigability, sub-clinical anemia too often does not receive corrective treatment until more serious symptoms urgently demand attention.

Frequently more than just iron deficiency is involved. The patient does not respond to simple iron therapy and other factors must be added.

Livitamin, "the first thought in hypochromic anemias," combines liver with iron and B complex vitamins, including vitamin B_{12}. Available as a palatable liquid or easily swallowed capsules, Livitamin provides a complete approach to the successful treatment of the hypochromic anemia syndrome.

Available on prescription in all pharmacies.

Write for sample and literature.

SE Mc Co

THE S. E. MASSENGILL COMPANY

Bristol, Tenn.-Va.

NEW YORK • SAN FRANCISCO • KANSAS CITY

Livitamin

LIQUID AND CAPSULES

Wider antibacterial range
...a safer sulfonamide

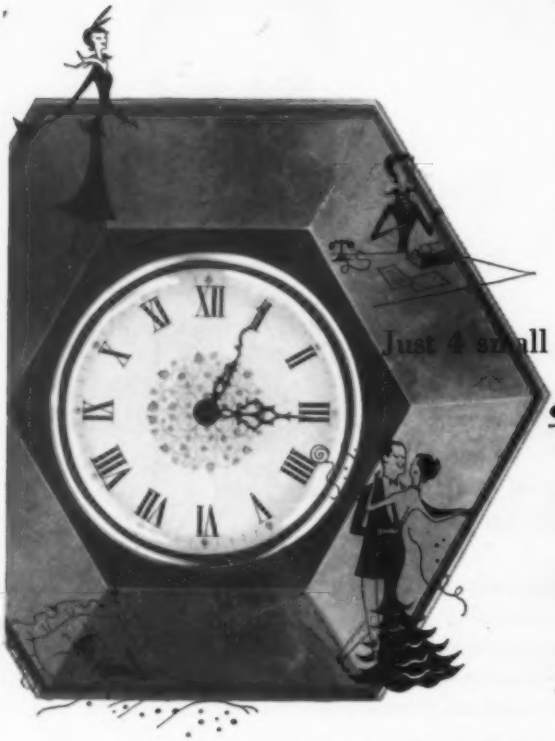
Gantrisin 'Roche' offers clinically important advantages in urinary and systemic infections. Because it is highly soluble —even in acid urine—Gantrisin eliminates the danger of renal blocking and obviates alkalinization. Gantrisin is a single sulfonamide, not a combination or mixture; its use therefore reduces the likelihood of allergic reactions. Gantrisin is distinguished by a wider antibacterial range; it has been effective in cases where antibiotics and other sulfonamides failed to produce results. Supplied in 0.5-Gm tablets, as a palatable syrup (0.5 Gm per 5 cc) and in 10-cc (4 Gm) ampuls.

HOFFMANN-LA ROCHE INC • NUTLEY 10 • N. J.

Gantrisin®

Brand of sulfisoxazole
(3,4-dimethyl-5-sulfanilamido-isoxazole)

'Roche'



Just 4 small doses provide

'Round-the-clock relief for allergic patients

Long-lasting relief[1] . . . low milligram dosage[2] with few side actions. These are advantages you *expect* in a professional antihistamine for use in difficult allergies, or for patients who have not responded to other drugs. These advantages are *combined* in Decapryn—the antihistamine that provides a good night's rest and a good day's work for allergic patients.

1 "Symptoms were relieved from 4 to 24 hours after the administration of a single dose of Decapryn—" . . . Sheldon, J.M. Et al: Univ. Mich. Hosp. Bull. 14:13-15 (1948)

2 "It was found that 12.5 mg. could be given during the day with comparatively few side reactions and yet maintain good clinical results—" . . . MacQuiddy, E.L.: Neb. State M.J. 34:123 (1949)

DECAPRYN®

The long-lasting, low-dosage prescription antihistamine

DECAPRYN (DOXYLAMINE) SUCCINATE

Merrell
1828
CINCINNATI • U.S.A.

Available on prescription only, as pleasant-tasting liquid, or palatable tablets

ACCEPTED

Good Citizenship

begins in the high chair!

THE effect of happy mealtimes on the development of a baby's complete personality is important. It can scarcely be overestimated.

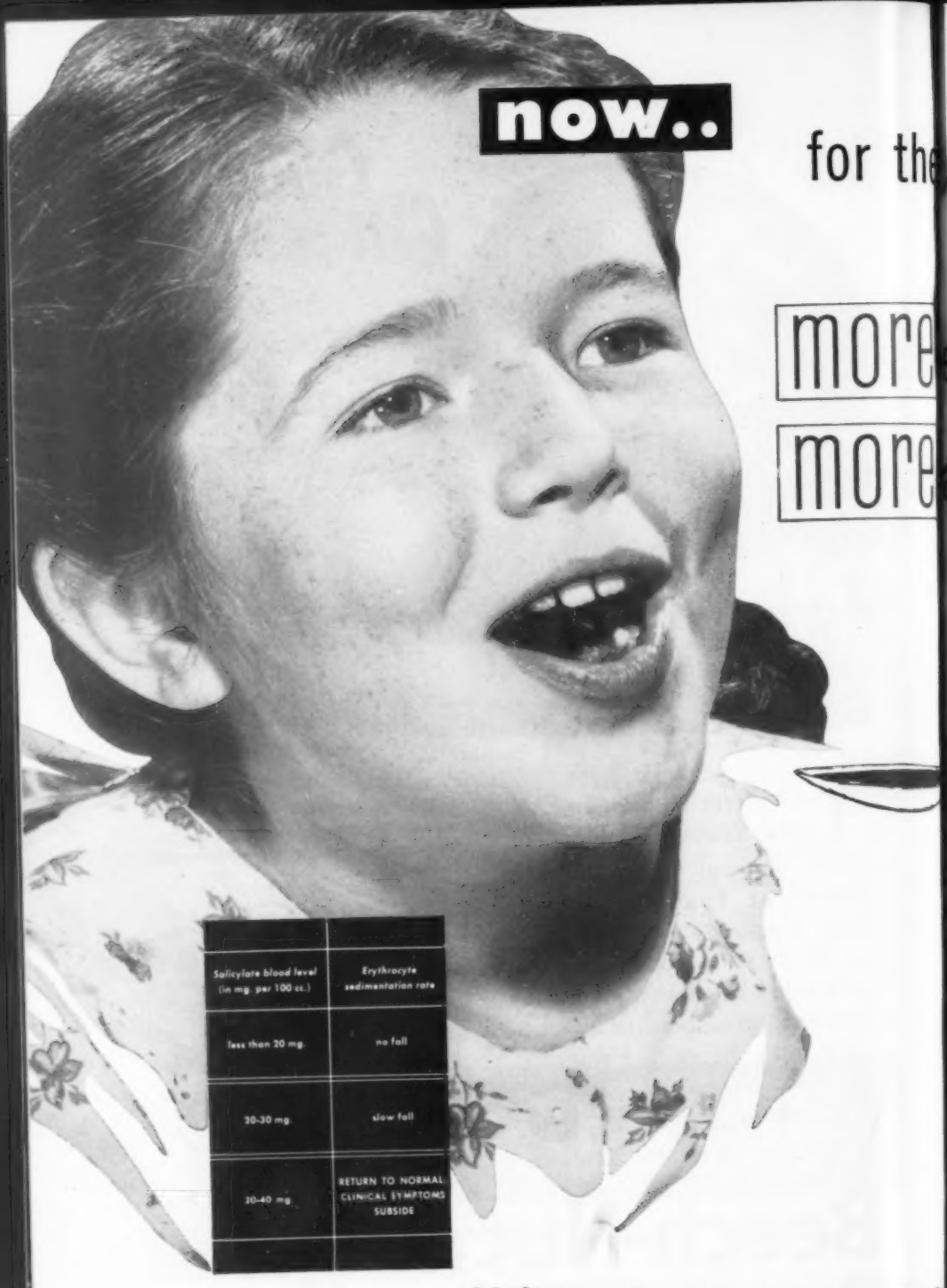
That's why mothers need to worry less about how *much* baby eats—and give more attention to how much he *enjoys* his meals! *Flavor-guarded* Beech-Nut Foods help baby get a good start nutritionally *and* emotionally.

A wide variety for you to recommend: Meat and Vegetable Soups, Vegetables, Fruits, Desserts — and Cereal Food.

All Beech-Nut standards of production and advertising have been accepted by the Council on Foods and Nutrition of the American Medical Association.

Beech-Nut FOODS for BABIES

Babies love them...thrive on them!

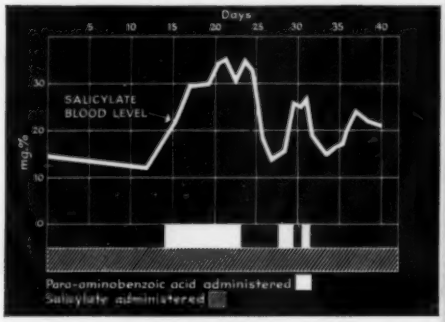

now..
for the
more
more
Salicylate blood level (in mg. per 100 cc.)
Erythrocyte sedimentation rate
less than 20 mg.
no fall
20-30 mg.
slow fall
30-40 mg.
RETURN TO NORMAL CLINICAL SYMPTOMS SUBSIDE
higher salicylate blood levels f

the *rheumatic* child

effective therapy in

acceptable form

*Para-aminobenzoic acid increases blood level of concurrently administered salicylate**



MORE EFFECTIVE THERAPY . . . since Pabalate supplies not only salicylate, but also the antirheumatic para-aminobenzoic acid, which acts (like a booster) to step up blood salicylate concentrations to those high levels so essential for real clinical efficacy. The salicylate, in turn, increases the blood levels of the para-aminobenzoic acid.

MORE ACCEPTABLE FORM . . . since Pabalate is available not only in Tablet form, but also as Pabalate Liquid, a chocolate flavored medication with a high degree of pharmaceutical elegance — appealing to the taste, and readily acceptable by even squeamish pediatric patients.

For better results, prescribe Pabalate — the "new word for salicylate" in antirheumatic therapy. Also valuable in analgesic or antipyretic therapy, in place of difficult salicylate tablet medication.

FORMULA: Each enteric coated tablet or each teaspoonful contains Sodium Salicylate, U.S.P. (5 gr.) 0.3 Gm.; Para-aminobenzoic Acid (as the sodium salt), (5 gr.), 0.3 Gm.

INDICATIONS: For the treatment of acute rheumatic fever or other rheumatic diseases in children, and as a replacement for salicylate tablet therapy.

A. H. ROBINS CO., INC. • RICHMOND 20, VA.

Ethical Pharmaceuticals of Merit since 1878

*Dry, T. J., et al.: Proc. Staff Meetings Mayo Clinic, 21:497, 1946.

For treatment of rheumatic affections

Rx *Pabalate*®

Robins

Is f*etter* antirheumatic therapy

THE GORDON ARMSTRONG COMPANY, INC.

Dear Doctor:

ABOUT PRICES

I'm writing you this memo October 9th to appear in all of our December advertising. By the time you read it anything can have happened but regardless of conditions in December our basic thinking will be the same. We shall fight against any increase in our selling price. This goes for any product we design and sell and applies particularly to the Armstrong X-4 Baby Incubator.

For 7 years now we have done this and in 7 years we have increased our Baby Incubator price less than 3 and ½ per cent and we have sold over 12,000 Baby Incubators. That's a record we're proud of. We shall keep on fighting costs.

Here is our pledge to you. We will not increase the price of the Armstrong X-4 Baby Incubator except as a last resort. As time goes on we may be forced to because we simply can't help it but we do not see it yet and we shall continue to fight against it.

Don't be "panicked" into buying anything. Don't order Armstrong X-4 Baby Incubators just because some other prices are going up. When you need Baby Incubators then buy an Armstrong X-4 because the price is low, because it is so easy to operate, because it is simple and safe and because back of every Armstrong X-4 Baby Incubator is 12,000 Incubators worth of experience.

We're both washing our necks in the same bucket you know—we're in this fight together. You can help us win by continuing to give us your loyalty and support just as you have for the past 7 years. Trust us to do our part.

Sincerely yours,

The Gordon Armstrong Company, Inc.

Gordon Armstrong
Pres-Treas

WHEN the Armstrong X-4 Baby Incubator was designed, we worked to keep both costs low for Armstrong X-4 users.

Low *first* cost has been accomplished by the elimination of unnecessary selling expense. Savings we have made in selling costs are passed along to X-4 users by holding down the price. As a matter of fact our price has increased less than 4% in seven years.

Low *operating* cost is accomplished through clean, simple design and easy control, with replacement parts for those that wear out in normal use available at low prices.

But these factors do not mean that the X-4 is cheap in *any* sense. All important construction materials and controls used throughout the X-4 are the finest on the market.

So, remember, the first cost on an X-4 is low, the operating cost is low. As long as it is humanly possible, we intend to keep it that way, as the users of over 12,000 Armstrong X-4 Incubators will tell you. Write for a complete description of the X-4 and you'll quickly realize why.

ACCEPTED COUNCIL ON PHYSICAL MEDICINE AMERICAN MEDICAL ASSOCIATION

THE GORDON ARMSTRONG COMPANY, INC.

Division PP-1 Bulkley Building, Cleveland 15, Ohio

Distributed in Canada by Ingram & Bell, Ltd.
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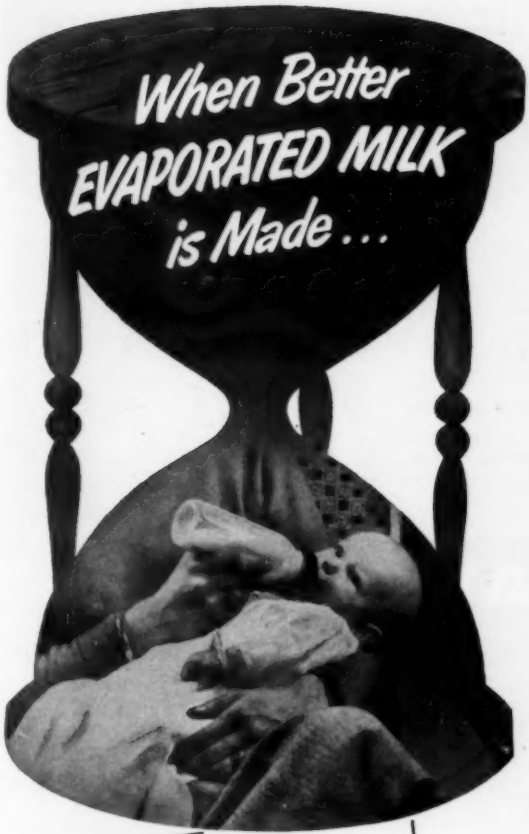
UL

"Back of every Armstrong X-4 Baby Incubator is over 12,000 incubators' worth of experience."

© The Gordon Armstrong Co., Inc.



Sixty-five years ago, the first completely safe milk for babies—evaporated milk—was developed by Pet Milk Company. The new process destroyed the germs of disease which often made cows' milk a dangerous food for babies.

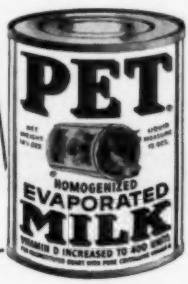
At the same time, Pet Evaporated Milk proved to be more easily digested than other forms of milk. Heat sterilization so changed the nature of the protein that it became soft and friable, resembling human milk in digestibility.

Then, Pet Milk was homogenized to distribute its butterfat evenly. Every drop was made uniformly rich in *all* the food values of milk.

When research proved that addition of vitamin D to milk would prevent rickets and promote optimal growth, Pet Milk was fortified with the recommended level of 400 units of vitamin D to the quart.

Later, when pure crystalline vitamin D_3 was developed Pet Milk was the *first* to use this improved form of vitamin D for the fortification of milk.

As it has for sixty-five years, Pet Milk Company will continue to look for new ways to improve its product . . . and contribute to the nutritional welfare of the nation—especially the nation's babies. Constant research is one of many reasons why the medical profession can be assured that *when better evaporated milk is made,* Pet Milk Company will make it!



Favored Form of Milk for Infant Formula

PET MILK COMPANY, 1437-L Arcade Building, St. Louis 1, Mo.

Background FOR GROWTH

"Young people of this country are taller and heavier than were the children of former years . . ."[1]

Contributing to better nutrition for infants and children all through their growing years is the combination of vitamins exhibited in

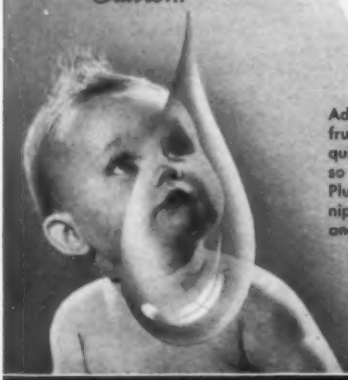
PLURAVIT® DROPS

8 Dispersible Vitamins Including Drisdol

Fully Utilized...
Easily Administered...
Stable...

A daily dose of 0.6 cc. provides:

VITAMIN A	5000 U.S.P. Units
VITAMIN D_2	1000 U.S.P. Units
VITAMIN B_1	1.0 mg.
VITAMIN B_2	0.4 mg.
VITAMIN B_6	1.0 mg.
VITAMIN C	50.0 mg.
NICOTINAMIDE	5.0 mg.
PANTOTHENIC ACID	2.0 mg.



Added to the infant's formula, water, milk, cereal, fruit juice or children's beverage, Pluravit Drops quickly become dispersed in liquid or solid foods so that utilization of the full dose is assured. Pluravit Drops do not float or adhere to bottle or nipple. Quick, uniform dispersion minimizes taste and aids absorption.

SUPPLIED IN BOTTLES OF 15 cc. WITH DROPPER

Winthrop Stearns Inc.
New York, N.Y. Windsor, Ont.

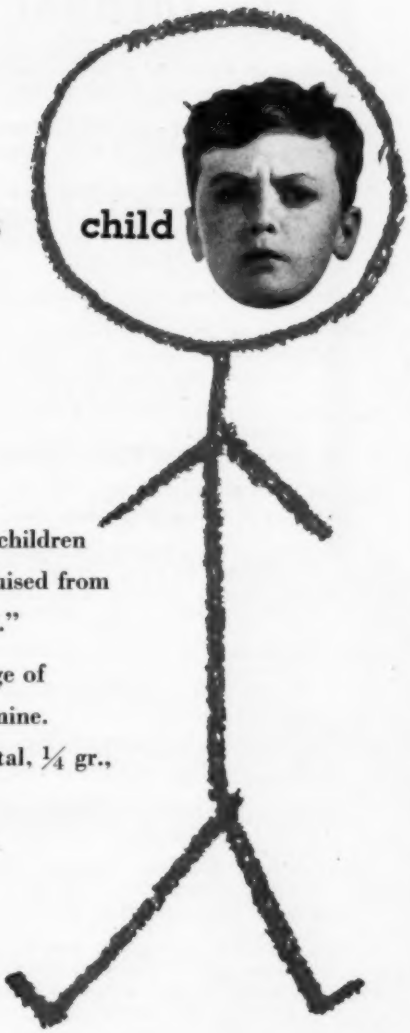
Pluravit and Drisdol, trademarks reg. U. S. & Canada
1. Jeans, Philip C.: Handbook of Nutrition, Chicago, American Medical Association, 1945, p. 384.

PLURAVIT DROPS *Pleasing Citrus Flavor* FOR INFANTS—GROWING CHILDREN

a superior presentation of

phenobarbital

for the tense and nervous child



Eskaphen B Elixir is pleasant and easy for children to take. Its barbiturate content is well disguised from parents who "know all about phenobarbital."

Eskaphen B Elixir has the further advantage of providing truly therapeutic dosages of thiamine. Each 5 cc. teaspoonful contains phenobarbital, ¼ gr., and thiamine, 5 mg.—*nearly three times the recommended daily allowance of thiamine.*

Smith, Kline & French Laboratories

Eskaphen B Elixir

the delightfully palatable combination of phenobarbital and thiamine

'Eskaphen B' T.M. Reg. U.S. Pat. Off.

Articles to appear in early issues of

The JOURNAL OF PEDIATRICS

AUREOMYCIN IN PEDIATRICS: A REVIEW.
By H. Shwachman, M.D., G. E. Foley, M.D., and C. D. Cook, M.D., Boston, Mass.

THE RELATIONSHIP BETWEEN INFANT FEEDING EXPERIENCE AND LATER BEHAVIOR.
By Niles Rumely Newton, M.A., Philadelphia, Pa.

POLIOMYELITIS IN THE EARLY NEONATAL PERIOD: REPORT OF A CASE OF POSSIBLE INTRAUTERINE INFECTION.
By Alexis Shelokov, M.D., and Louis Weinstein, M.D., Boston, Mass.

HYDROCEPHALUS.
By Allan Bloxsom, M.D., Houston, Texas.

LATER STATUS OF JUVENILE DIABETICS.
By C. William Daeschner, M.D., Robert W. Deisher, M.D., and Alexis F. Hartmann, M.D., St. Louis, Mo.

SALMONELLA BAREILLY MENINGITIS IN A CHILD SUCCESSFULLY TREATED WITH INTRAVENOUS AUREOMYCIN.
By Emanuel Padnos, M.D., and Milton Goldin, B.S., M.S., Chicago, Ill.

RESULTS OF HISTOPLASMIN SKIN TESTING IN CHILDREN FROM THE ST. LOUIS, MO., AREA.
By John F. Lynch, M.D., High Point, N. C., and E. Bryce Alpern, M.D., Detroit, Mich.

AN EVALUATION OF A CARBOHYDRATE-PHOSPHORIC ACID SOLUTION IN THE MANAGEMENT OF VOMITING.
By J. Edmund Bradley, M.D., Leah Proutt, B.S., E. Roderick Shipley, M.D., and Robert H. Oster, Ph.D., Baltimore, Md.

ELECTROCARDIOGRAPHIC CHANGES OCCURRING DURING THE COURSE OF REPLACEMENT TRANSFUSIONS.
By Robert A. Furman, M.D., Herman K. Hellerstein, M.D., and Viola V. Startzman, M.D., Cleveland, Ohio.

SOME INTERVIEW TECHNIQUES IN CHILD PSYCHIATRY.
By Hyman Caplan, M.D., New York, N. Y.

A REVIEW OF THE SURGICAL TREATMENT OF INTERNAL HYDROCEPHALUS.
By Ira J. Jackson, M.D., Galveston, Texas.

RETROLENTAL FIBROPLASIA. CLINICAL STATISTICS FROM THE PREMATURE CENTER OF THE CHARITY HOSPITAL OF LOUISIANA AT NEW ORLEANS.
By A. L. Exline, Jr., M.D., and M. R. Harrington, M.D., Philadelphia, Pa.

A CLINICAL STUDY CONCERNING THE VALUE OF BIOLAC. III. EFFECT OF CHANGES INTRODUCED IN NEW IMPROVED BIOLAC UPON GROWTH OF YOUNG INFANTS.
By Sprague Hazard, M.D., and Clement A. Smith, M.D., Boston, Mass., and Florence Denton, A.B., Oakland, Calif.

AURICULAR SEPTAL DEFECTS IN CHILDREN.
By John D. Keith, M.D., and Constance C. Forsyth, M.D., M.R.C.P., Toronto, Canada.

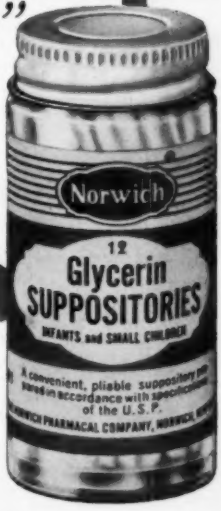
TOTAL ABSENCE OF THE CEREBRAL HEMISPHERES.
By Eloise Eberling Johnson, M.D., Mary Warner, M.D., and J. P. Simonds, M.D., Chicago, Ill.

METHYLENE BLUE IN THE TREATMENT OF METHEMOGLOBINEMIA IN PREMATURE INFANTS CAUSED BY MARKING INK.
By James N. Etteldorf, M.D., Memphis, Tenn.

What every young mother should know ...but often doesn't

we tell her in PARENTS' MAGAZINE

When your doctor says "glycerin suppositories" say "Norwich" to your druggist



for "Norwich" means

- a U.S.P. product—with ingredients protected for purity by Norwich laboratory-control.
- a prompt, gentle aid in cases of temporary constipation.
- made especially for infants—pliable, precisely tapered, uniform.

COMMENDED BY THE PARENTS' MAGAZINE

Now... ANOTHER FINE Norwich® PRODUCT FOR CHILDREN

CHILDREN'S ASPIRIN
Accurate dosage, 1¼ grains
(¼ the usual U.S.P. tablet)

Palatable—Colored, easy to administer.

COMMENDED BY THE PARENTS' MAGAZINE

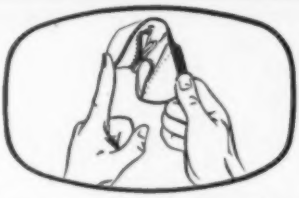
FREE to Profession
Full-size bottles of new Norwich Children's Aspirin and Infants' Glycerin Suppositories. Request on letterhead or coupon below.

The Norwich Pharmacal Company, Norwich, New York
Send 2 Norwich products for children. (PLEASE PRINT)

Dr. _____

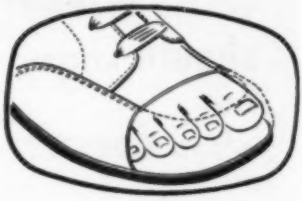
Address _____

City _____ State _____



COMPLETE

Flexibility . . .



. . . PLENTY OF TOE ROOM

Those are the reasons why so many pediatricians approve of Self-Starters as "start to six" shoes for normal feet. They mean that every pedal bone and muscle is not only permitted but encouraged to function, grow and develop perfectly naturally, thus laying the foundation for lifelong foot health and comfort.

You, too, should be familiar with these scientifically designed, perfect fitting shoes. Write for descriptive literature and name of nearest experienced Self-Starter fitter.

THE CARPENTER SHOE COMPANY, INC.
161 CLARISSA STREET, ROCHESTER 8, N. Y.

Self-Starters
BY CARPENTER

HYLAND IMMUNE SERUMS

HUMAN • DRIED

Mumps Immune Serum

IRRADIATED

Obtained from healthy adults who have been hyperimmunized with mumps virus vaccine.

Hyland Irradiated Mumps Immune Serum may be administered intramuscularly or intravenously.

Confers passive immunity for approximately 10 to 14 days. If exposure continues, immunity may be sustained by repeating dosage.

In the treatment of mumps, there is some evidence that the serum prevents serious complications if administered early in adequate amounts.

Pertussis Immune Serum

IRRADIATED

Obtained from healthy adults who have been hyperimmunized with pertussis vaccine.

Hyland Irradiated Pertussis Immune Serum may be administered intramuscularly or intravenously.

Confers passive or protective immunity for approximately 10 to 14 days. The dose is 20 cc. for young children and more for older children or adults. The dose may be repeated as indicated.

In treatment the dose must be greater than the prophylactic dose and repeated as indicated by the clinical course.

No preservative added, but treated with ultraviolet radiation. Dried for stability, simple to administer. Both AVAILABLE—20 cc. dried serum with suitable diluent.

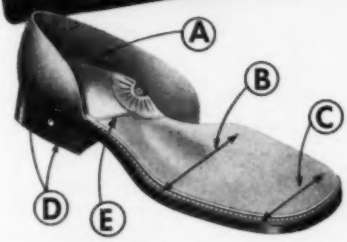
HYLAND LABORATORIES

BIOLOGICALS

4534 Sunset Boulevard, Los Angeles 27, California • 26 Vark St., Yonkers 1, New York

Child Life

ORTHOPEDIC SHOES FOR CHILDREN



A **LONG INSIDE COUNTER,** molded to the last, gives added support to prevent pronation.

B **SCIENTIFICALLY DESIGNED METATARSAL AREA,** correctly supports and aligns the metatarsals; extra width at ball allows freedom of foot action. No crowding, no cramping, no constriction of nerves or muscles.

C **BROAD TOE AREA,** room for toes to grow straight and strong with no interference to free function.

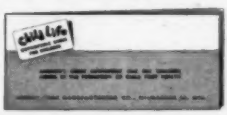
D **ANTI-SLIP HEEL AND THOMAS WEDGED HEEL** for better heel and longitudinal arch support.

E **STRONG LONGITUDINAL ARCH SUPPORT** to prevent pronation or eversion, helping balanced foot function.

AIDING YOU IN THE PROMOTION OF CHILD FOOT HEALTH

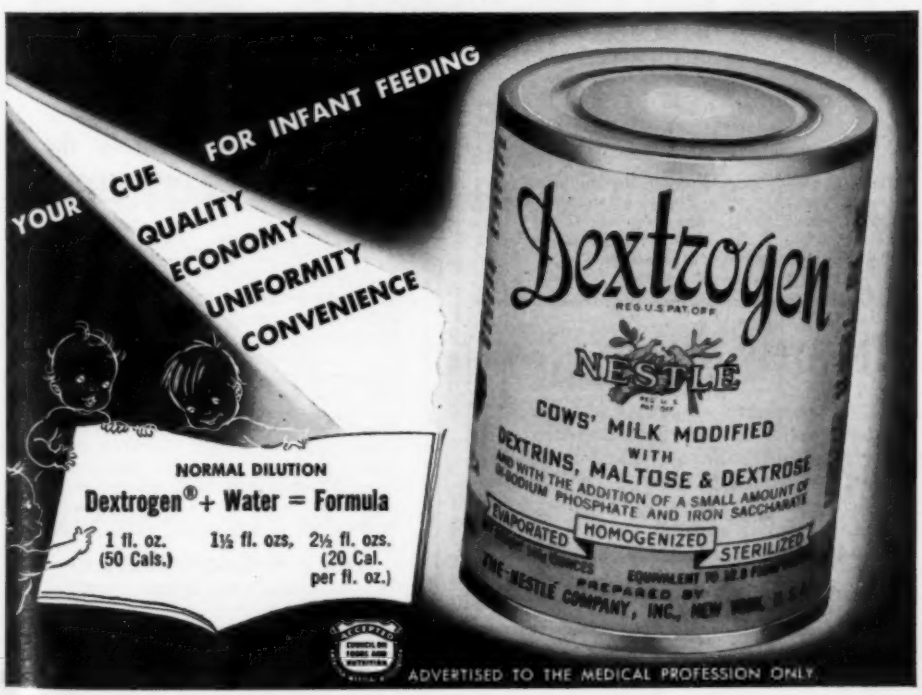
CHILD LIFE Shoes are the result of decades of study and research. CHILD LIFE lasts, patterns, counters, shank pieces and heels are orthopedically designed . . . with patterns coordinated to each last, size-for-size and width-for-width. CHILD LIFE Shoes are not "cure-alls" but they will definitely help in re-establishing proper balance and unhampered function for feet which have become pronated. There are 20 CHILD LIFE ORTHOPEDIC STYLES IN STOCK, in all sizes and widths.

CHILD LIFE Orthopedic Shoes, because of their firm foundation, assist in postural and functional correction.



Write for Your Copy of the CHILD LIFE Booklet showing shoes and special features, and Authentic Wedge Chart.

HERBST SHOE MFG. CO., Milwaukee 45, Wis.



Edwards

REGULAR AND CORRECTIVE SHOES FROM TOTS TO TEENS

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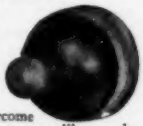

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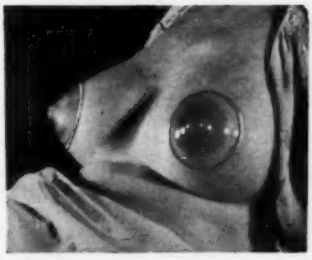

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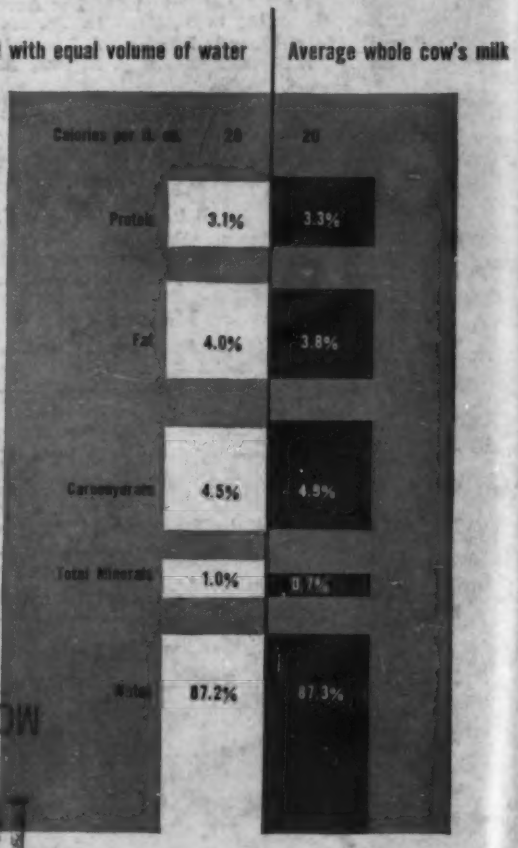

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